AD

Award Number DAMD17-99-1-9049

TITLE: Race/Ethnic Based Genetic Variations in Human Genes:
Defining the Genetic Evidence for Disparity of Prostate Cancer
Risk and Mortality Between Different Populations

PRINCIPAL INVESTIGATOR: John Franklin, M.D.

CONTRACTING ORGANIZATION: Columbia University

New York, New York 10032

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FOREWORD

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For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

Research Council (NIH Publication No. 86-23, Revised 1985).

 $N \mid \Omega$ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

NB In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

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PI - Signature

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INTRODUCTION:

Prostate cancer incidence and mortality rates are significantly higher for African-American men than for men of other ethnic groups. The increased risk of prostate cancer observed among African Americans appears to extend more generally to African blacks. This difference is not simply a function of differential access to medical care. Therefore, there is likely to be a genetic basis for this disparity. Several hot spots for genetic variation to identify the basis for this prostate cancer disparity have been investigated. Among these, the vitamin D receptor and the androgen receptor have already shown promise. Variations in genetic polymorphisms have also been identified among blacks and whites in the apolipoprotein-J/clusterin (APOJ/CLI) gene. The protein product of the APOJ/CLI gene is associated with programmed cell death observed when prostate cancer cells undergo apoptosis following androgen withdrawal. No study, to date, has reported on the variability of genetic polymorphism of the apolipoprotein-J/clusterin gene and differences in prostate cancer risk between blacks and whites. The purpose of this research proposal is to determine if certain genetic variations in the androgen receptor gene, the vitamin D receptor gene, or the apolipoprotein-J/clusterin gene can distinguish African American populations from other ethnic varieties and whether the occurrence of particular genetic variations in either of these three genes might correspond to a higher risk for prostate cancer occurrence and mortality in the African American population under study. To achieve these objectives, the goal of applicant has been to design a research program, which utilizes the patient and laboratory resources available at the New York Presbyterian Hospital. The scope of this research is far reaching. The applicant will be able to assess the feasibility of subject accrual and specimen collection in the targeted minority populations. The prevalence of genetic polymorphisms of interest in the targeted populations will be determined. With this information, appropriate sample sizes and power analyses can be carried out to plan a large-scale study to assess the a priori hypothesis that the racial disparities in prostate cancer risk and mortality are due to genetic environmental interactions. Understanding the basis for the adverse prostate cancer risks faced by African-American men could lead to interventions including behavioral modifications, nutritional supplements, or therapies.

BODY:

Below I describe the research accomplishments associated in each task outlined in the approved Statement of Works:

Statement of Work

Phase 1: Project Startup and Parameter Development

Meet with collaborating established investigators

Central to the design of the research program is a collaborative relationship with Dr Ralph Buttyan and Dr. Alfred Neugut. Dr. Buttyan is an established investigator in the field of prostate cancer research, and is the Director of the urology research laboratory at Columbia University. Dr. Neugut is an experienced cancer epidemiologist with joint appointments in both the Department of Medicine and the School of Public Health at Columbia University. The applicant met regular with both established investigators to develop the structural design of the project. The basic design is that of a cross-sectional study.

 Meet with attending staff in the departments of urology and radiation oncology to establish source of subjects

See, Appendix 1: Letters of Support.

A letter of support was obtained from Dr. Errol Mallet, who is the senior community urology in a large group practice in Brooklyn and Queens, New York. This group of urologists primarily serves the Caribbean population in these boroughs. A letter of support has also been obtained from Dr. Gerald Hoke, a urologist serving the black American population of Harlem, New York. In addition, letters of support have been obtained from the Departments of Medical Oncology and Radiation Oncology.

The Principal investigator will have access to his target populations through the resources available at the Columbia-Presbyterian Medical Center in New York. In specific, the Principal investigator will have access to a general urology clinic at the Allen Pavilion and a multi-disciplinary urology clinic the Atchley Pavilion. The Allen Pavilion, located in a large Hispanic community, was incorporated into Columbia-Presbyterian Medical Center to enhance the institution's services to this community. The Allen Pavilion will be primary resource access to the non-white Hispanic male population. The Principal investigator will have access to a large local population of geographically diverse men of African descent (African-American as well as African-Caribbean) through his contacts with Harlem Hospital and community urologists in Brooklyn and Queens.

• Purchase a data management program

Dell Laptop computer has been purchased as well as a SAS statistical program.

• File an application for IRB approval

An IRB proposal was written and submitted, and a final approval is pending (See Appendix 2).

• Enroll in epidemiology and biostatisical courses

Enrolled in advanced Epidemiology and Sociomedical Science core courses during the Spring, 1999 semester.

Phase 2: Information Consolidation and Project Development through Consultative Interactions.

• Collect specimens and develop PCR analytical procedures in laboratory

Awaiting IRB approval to begin collection of samples.

• Communicate with international contacts

Communicated with Dr. Lawson Douglas, Director of Urology, University of the West Indies, Jamaica, and Dr. Alex Danso of Harare Zimbabwe. When I met with Dr. Lawson Douglas in Jamaica, at the annual Nov. 1998 Caribbean Urologic Convention, he once again gave me his support to contribute subjects to the study. Correspondence with Dr. Alex Danso, of Harare Zimbabwe has resulted in a commitment of support. Dr. Danso also reconfirmed his commitment to contribute subjects to the study when I met with him in May 1999, during his visit to the United States. See Appendix 3.

• Begin body of application for formal grant (RO1 or other)

A second proposal was submitted to the DOD PCRP for a Minority Population Focussed Collaborative Training Award (PC991287) (Appendix 4). This proposal will focus on the collection of samples and laboratory analysis in order to obtain pilot data to support an application for a formal grant (RO1 or other).

The applicant also attended the FASEB Phase I Grantwriter's Seminar in Tucson, Arizona, and submitted an application for the Phase II Seminar in the Fall of 1999. (Appendix 5)

A questionnaire to assess subject's personal and family history was developed from modifications to the Metropolitan New York Registry Personal History Male Questionnaire and a Demographic Questionnaire obtained from Carol Magai, Ph.D., Dean of Research, Long Island University, Brooklyn Campus (See Appendix 6). This survey was pilot tested.

The Diet Questionnaire developed by the Epidemiology Program Cancer Research Center of Hawaii, University of Hawaii will also be used to assess diet information. (Appendix 7)

Phase 3: Formulation of Research Questions for Formal Grant

Formulation of research questions for a formal grant is being developed. Upon IRB approval experimentation will be initiated.

KEY RESEARCH ACCOMPLISHMENTS:

- Developing relationships with community and institutional contacts that will allow the applicant to successfully recruit the targeted populations.
- Developing a pilot tested survey to assess subject's personal and family history, and acquiring a validated diet survey.
- Fostering international contacts.
- Developing extended mentoring relationships outside of the key collaborators.

REPORTABLE OUTCOMES:

- Submitted a DOD PCRP MPFCTA proposal (Appendix 4).
- Completed 2 courses towards MPH degree in epidemiology.

CONCLUSIONS:

Black American men are adversely affected by prostate cancer compared to white American men. A genetic basis for this disparity is suspected. The applicant has designed a research program to assess the relationship of ethnic/racial genetic polymorphisms in the androgen receptor gene, the vitamin D receptor gene, and the APOJ/CLI gene and the ethnic racial disparities among black and white men. The applicant has established a solid foundation upon which these research objectives can be pursued. An IRB proposal has been submitted, and an application for funding to support the initiation of experimentation has also been submitted. Pilot data obtained from the next phase of this project will be utilized to support a formal grant proposal. This research has the potential to shed further insights into the causes of the prostate cancer disparities observed among black and white males.

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Alfred I. Neugut, M.D., Ph.D. Department of Medicine & The Joseph L. Mailman School of Public Health Columbia University 600 West 168th Street New York, New York 10032

Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 1



College of Physicians and Surgeons of Columbia University Columbia-Presbyterian Medical Center

Columbia Presbyterian Medical Center Atchley 919 161 Fort Washington Avenue New York, N Y 10032-3789

Daniel P. Petrylak, M.D. Asst. Professor of Medicine Director, Genitourinary Oncology Program Division of Medical Oncology

> Tel: (212) 305-1731 Fax: (212) 305-6762 E-Mail:dpp5@columbia.edu

March 6, 1999

John Roland Franklin, M.D. Department of Urology Allen Pavilion

Dear John:

Congratulations on your receiving the DOD Award to evaluate the genetic role of variations in prostate cancer risk and mortality among different racial populations. I very much like your propsal and am excited about contributing potential subjects to this project.

I look forward to working with you. Please let me know if I can be of further assistance.

Sincerely,

Daniel P. Petrylak, M.D.

60 PLAZA UROLOGY ASSOCIATES 60 PLAZA STREET SRODKLYN. N. Y. 11238 638-9222 FAA 638-9257

March 8, 1999

John R. Franklin, M.D. College of Physicians and Surgeons of Columbia University

Dear Dr. Franklin,

The letter is to confirm our commitment and to express support to your proposed study evaluating genetic polymorphisms in a number of genes including the CAG/GGC of the androgen receptor gene and the APO/Clusterin gene

Of major interest to you is the fact that our group serves an african-american and caribbean population. We have and continue to screen and treat a large number of caribbean men with prostate cancer.

I wish you all the success in this important endeavor and assure you of all the support my associates and I can offer you

Sincerely yours,

FM.

Errol C Mallett M.D., F.A.C.S.



The Presbyterian Hospital in the City of New York Columbia-Presbyterian Medical Center, New York, NY 10032-3784

March 5, 1999

John R. Franklin, M.D. Department of Urology

Dear John:

I am excited to hear about your proposed project studying the genetic basis of the disparity of prostate cancer risk and mortality between different racial populations. I have reviewed you proposal and think that this is an excellent project. I would be enthusiastic about enrolling patients in this study. I look forward to helping you with this project. If you have any further questions, please do not hesitate to contact me at any time.

Sincerely,

Ronald D. Ennis, M.D.

RDE:jc

COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS & SURGIONS HARLEM HOSPITAL CENTER

DEPARIMENT OF SURGERY

March 8, 1999

Dr. John Franklin Allen Pavilion Presbyterian Hospital 5420 Broadway New York, New York

Dear Dr. Franklin:

I have read your research proposal regarding Racial Disparity In Prostate Cancer, and I am willing to participate in your study. I can assist you by providing prostate cancer patients from Harlem Hospital Center as well as patients from my private practice at the New York Presbyterian Hospital.

Sincerely,

Gerald Hoke Gerald P. Hoke, MD MPH

Chief of Urology

GPH/bd

506 Lenox Avenue New York, NY 10037

Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 2

COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS & SURGEONS

COLUMBIA-PRESBYTERIAN MEDICAL CENTER INSTITUTIONAL REVIEW BOARD

CPMC IRB

July 12, 1999

- .

John Franklin, M.D. Department of Urology Atchley Pavilion - 11th floor

Re: IRB #9049, RACE/ETHNIC BASED GENETIC VARIATIONS IN HUMAN GENES: THE GENETIC EVIDENCE FOR DISPARITY OF PROSTATE CANCER RISK AND MORTALITY BETWEEN DIFFERENT POPULATIONS

Dear Dr. Franklin:

Company of the second of the s

I am writing to confirm that this study is currently being reviewed by the $\ensuremath{\mathsf{CPMC}}$ Institutional Review Board.

The CPMC IRB Assurance # is M1356 01.

Please let me know if the Department of Defense needs any other information about the IRB's review of this study.

Sincerely,

Judith Jansen

IRB Administrator

JJ/jrj

Marilyn Wallace
Assistant Director
Grants & Contracts
Health Science

Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 3

From: Dr Danso <danserv@harare.iafrica.com>

To: Cathy Franklin < jcfranklin@worldnet.att.net>

Date: Saturday, November 28, 1998 3:53 AM

Subject: Re: Prostate cancer research

My dear John,

I am sorry I have not been able to write earlier but believe you me, I have been thinking of you all every minute of the day. I am so happy that Asantewa is growing and becoming a big girl. I shall be able to collaborate on the research programme that you have started. Just let me know so that we can give you our input.

For the past three years as you know I have not been doing too much of the urological conferences . i had to see the boys through college and this is a whopping 60thousand dollar bill a year. Living and working in Africa it gives you no further room economically to manoevre . But Thank God , Kwabena is finishing next year . Oh how time flies !!.

The news I have for you is that I have been involved in a group which is getting an international hospital built in Accra!. The private placement document for that project has just been brought out . you cannot imagine how hectic this has been and infact I have been going to Ghana every four weeks. We acquired a 20acre piece of land in Accra and got some architects to do the drawings . The feasibility study was finished a year ago and I have been running all over the show with it . The investors have started putting in money and the construction is starting in 8weeks time . We have sunk a lot of effort and resources into this and now it is taken off . The flotation of the shares has just started so if you want to invest in Africa , there you are . We haven't met for a very long time and I am hoping that we shall meet , next year . God willing.

Mary and I are well and extremely excited at the Accra International Hospital and the fact that it has taken off so well. There is a provision for telemedicine and I am speaking to Johns Hopkins and UCIA for help. We shall be leaving for Accra on the 23rd of December to spend the Christmas at home and this year we shall be spending it as a full family because the boys are meeting us in Ghana.

Cathy , Kwabena is finishing in May 1999and would be majoring in Math and economics , please give him some guidance because he would like to go to business school. my thinking was for him to come to Africa for a few years before going to do the MBA but he is not keen in returning to Africa and yet remaining in the US and doing a good job is most difficult . Please do guide us all now and then when you have the time .

We are all dying to see you and especially Asantewa. my love to all of you

Best of wishes . Love Danso .

From: Cathy Franklin < jcfranklin@worldnet.att.net > To: Alex Danso < danserv@harare.iafrica.com >

Subject: Prostate cancer research

Date: Monday, October 19, 1998 5:16 PM

Hi Alex,

How are you and Mary? It was real nice hearing from you both. Cathy, Asantewa, and I are going through all the growing pains of a working family with a young child. My experience at Columbia University is beginning to take some shape. As you know it does take time to build a practice. I have been awarded a Department of Defense Grant to do a pilot project. I propose to evaluate the genetic basis of the racial/ethnic differences of prostate cancer. I am looking at the CAG gene, the Vit D gene, and the APO J/Clusterin gene among others. I have propose not only to look at differences between whites and blacks, but also to look at differences between black Americans and blacks from the Caribbean and Africa. I have listed you as one of my contact persons in Africa for collaboration and for potential samples. I am now in the process of writing my IRB proposal so that I can get started.

This is an ambitious project. I have secured to support of Dr. Olsson as well as the director of the urology research lab (Dr. Ralph Buttyan) and an established cancer epidemiologist (Dr. Alfred Neugut). Dr. Neugut is an Associate Professor with the Columbia University School of Public Health. I look forward to discussing this project with you some. As you can see, Alex and Mary, our lives have gotten real busy/crazy. In addition to getting the research of the ground I am doing my MPH in epidemiology. But then again Alex, you are planning or have begun to pursue a MBA Ha! Ha! I think that if we continue to apply ourselves to the cause we will get somewhere.

Love always

John and Family.

Asantewa had a wonderful time for her birthday. She cried when we sang the Happy Birthday song.

Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 4

Peer Review Referral Page:

Proposal Title: Assessment of Genetic Variations among Different Ethnic/Racial Groups: An Explanation of Ethnic/Racial Disparities in Prostate Cancer Risk and Mortality.

Principal Investigator: John R. Franklin, M.D.

Keyword Descriptive Technical Terms:

Cancer biology, Epidemiology/Biostatistics, Molecular Genetics, Prostate cancer risk, Prostate cancer mortality, Ethnic/racial disparity, Genetic polymorphisms.

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Proposal Title Page:

Proposal Title: Assessment of Genetic Variations among Different Ethnic/Racial Groups: An Explanation of Ethnic/Racial Disparities in Prostate Cancer Risk and Mortality.

Award Category: Minority Population Focused Collaborative Training Awards

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Proposal Start Date: July 1, 1999

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Abstract: (technical)

<u>Title:</u> Assessment of Genetic Variations among Different Ethnic/Racial Groups: An Explanation of Ethnic/Racial Disparities in Prostate Cancer Risk and Mortality.

Principal investigator's name: John Roland Franklin, M.D. Department: Urology

Study purpose

Prostate cancer occurs more frequently among black males than it does among white males. Black males also have twice the risk of dying from prostate cancer than do white males. The purpose of this study is to determine whether differences in certain human genes can explain why black males are more adversely affected by prostate cancer than white males. The study will evaluate variations in the following genes by amplifying specific DNA segments from certain genes utilizing a commonly used technique called the Polymerase Chain Reaction (PCR). The genes of interest are the androgen receptor gene, the vitamin D receptor gene, the APOJ/clusterin gene, the CYP3A4 gene, and the SRD5A2 gene. In the study men will be selected from the following ethnic/cultural populations: white, black American, black Caribbean, black continental African, and non-white Hispanic. By conducting statistical analyses, associations between genetic markers in these genes and prostate cancer can be evaluated. Further assessments will be made to determine whether the higher risk of prostate cancer among black Americans can be explained by these genetic markers, and whether the same genetic risks exists in other black populations.

Study subjects and method of recruitment

We expect to enroll a total of 400 men in the initial phase of the study. One hundred men will be selected from each of the following ethnic groups: white men, black American, black Caribbean and non-white Hispanic. Fifty men from each population will be recruited because they have a diagnosis of prostate cancer. The remaining 50 men will be free of any known diagnosis of prostate cancer and will serve as controls. All men must be 50 years and older and must be competent to give an informed consent. Subjects will be recruited primarily at the New York Presbyterian Hospital. The attached letter will be sent to all urologist, radiation oncologists and medical oncologist at the New York Presbyterian Hospital for their support in the study. In order to recruit patients from the black American, Caribbean, and Hispanic populations, the attached letter will be sent to community urologist who primarily serve these populations.

Study Procedures: Men who are recruited to participate in the study will be required to sign an informed consent. The subjects will complete a questionnaire detailing their age, weight, ethnic background, date of diagnosis of prostate cancer, family history, etc. Thereafter, 1 to 2 tablespoons of blood will be obtained via a needle stick of a large vein on the arm. The blood will be coded and taken directly to the laboratory where it will be processed. These procedures will be performed during a single visit with a research representative. Data will then be stored in a computer database for subsequent statistical analysis.

Issues: Subject identity will be shielded in any publications or presentations made on the finding of this study. Subject identity may be revealed to any federal, state, or institutional regulatory body upon request. Blood extraction may be associated with pain, bleeding, or infection. Study finding will not be made available to the individual subjects.

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Proposal Abstract (non-technical)

Assessment of Genetic Variations among Different Ethnic/Racial Groups: An Explanation of Ethnic/Racial Disparities in Prostate Cancer Risk and Mortality.

Principal investigator: John Roland Franklin, M.D. Department: Urology

Study purpose

Prostate cancer occurs more frequently among black males than it does among white males. Black males also have twice the risk of dying from prostate cancer than do white males. The purpose of this study is to determine whether differences in certain human genes can explain why black males are more adversely affected by prostate cancer than white males. The study will evaluate discrepancy in specific genetic coding locations. This will be accomplished by increasing the amount DNA segments from the genes of interest utilizing a commonly used technique called the Polymerase Chain Reaction (PCR). The PCR is a mechanism designed to repetitively make specific genetic material. The genes of interest are the androgen receptor gene, the vitamin D receptor gene, the APOJ/clusterin gene, the CYP3A4 gene, and the SRD5A2 gene. In the study men will be selected from the following ethnic/cultural populations: white, black American, black Caribbean, black continental African, and non-white Hispanic. By conducting statistical analyses, relationships between genetic markers in these genes and prostate cancer risk and/or mortality can be evaluated. Further assessments will be made to determine whether the higher risk of prostate cancer among black Americans can be explained by these genetic markers, and whether the same genetic risks exists in other black populations.

Study subjects and method of recruitment

We expect to enroll a total of 400 men in the initial phase of the study. One hundred men will be selected from each of the following ethnic groups: white men, black American, black Caribbean and non-white Hispanic. Fifty men from each population will be recruited because they have a diagnosis of prostate cancer. The remaining 50 men will be free of any known diagnosis of prostate cancer and will serve as controls. All men must be 50 years and older and must be competent to give an informed consent. Subjects will be recruited primarily at the New York Presbyterian Hospital. The attached letter will be sent to all urologist, radiation oncologists and medical oncologist at the New York Presbyterian Hospital for their support in the study. In order to recruit patients from the black American, Caribbean, and Hispanic populations, the attached letter will be sent to community urologist who primarily serve these populations.

Study Procedures: Men who are recruited to participate in the study will be required to sign an informed consent. The subjects will complete a questionnaire detailing their age, weight, ethnic background, date of diagnosis of prostate cancer, family history, etc. Thereafter, 1 to 2 tablespoons of blood will be obtained via a needle stick of a large vein on the arm. The blood will be coded and taken directly to the laboratory where it will be processed. These procedures will be performed during a single visit with a research representative. Data will then be stored in a computer database for subsequent statistical analysis.

Issues: Subject identity will be shielded in any publications or presentations made on the finding of this study. Subject identity may be revealed to any federal, state, or institutional regulatory body upon request. Blood extraction may be associated with pain, bleeding, or infection. Study finding will not be made available to the individual subjects.

Statement of Work

Assessment of Genetic Variations among Different Ethnic/Racial Groups: An Explanation of Ethnic/Racial Disparities in Prostate Cancer Risk and Mortality.

Phase 1: Project Start-up and Parameter Development (Month 1-3)

- Meet with established investigators to review progress of collaborative effort
- Send letters to local contacts to formally request their support of subject recruitment
- Develop questionnaire or select appropriate questionnaire to ascertain necessary subject history including family history and dietary information
- Finalize procedures to ensure IRB approval
- Purchase laboratory supplies and materials
- Enroll in epidemiology course
- Continue to develop body of application for formal RO1 or other grant

Phase 2: Information Consolidation and Initiation of Data Collection (Month 4-8)

- Establish with collaborators mode of coding and data storage
- Begin enrolling subjects into study
- Collect questionnaire data
- Collect specimens and begin PCR analytical procedures
- Finalize RO1 or other grant for submission

Phase 3: Refine Research Questions for Formal Grant (Month 9-12)

- Continue subject enrollment and data collection
- Work with biostatistician to statistically analyze data
- Finalize preliminary experimentation results
- Prepare and submit report

Proposal Relevance and Impact Statement:

Prostate cancer remains the most common cancer affecting adult males in the United States, and is the second leading cause of cancer related deaths in this country. Black American men are disproportionately affected by prostate cancer with an incidence 50% higher than that of white American men. Even more alarming, black American men are twice as likely to die from prostate cancer than are white men. Issues such as access to health care do not completely explain these ethnic/racial differences in prostate cancer incidence and mortality. Still unknown is whether genetic factors, environmental factors or genetic environmental interactions can explain these disparities. Some evidence exists that describe ethnic/racial variations in a number of genes, which participate in prostate cancer metabolism. Among these genes are the androgen receptor, and the vitamin D receptor. Although ethnic/racial variations have been observed in the APOJ/CLI gene and the CYP3A4 gene, no studies to date have evaluated these genetic variations in men with prostate cancer. Clearly further research is needed to evaluate why black American men are more adversely affected by prostate cancer than are white American men. In this proposal the applicant intends to combine, in collaborative effort, clinical, basic science, and epidemiologic methodologies to explore the genetic, environmental factors that may be accounting for these racial disparities in prostate cancer risk and mortality.

The applicant has outlined the following objectives in his proposal: 1) to determine whether certain genetic variations in the androgen receptor gene, the vitamin D receptor gene, SRD5A2 gene, the CYP3A4 gene, or the apolipoprotein-J/clusterin gene distinguish African American populations from other ethnic varieties. 2) To assess whether the occurrence of particular genetic variations in any of these five genes might correspond to a higher risk for prostate cancer occurrence and mortality in the African American population. 3) To evaluate if there is any relationship in the occurrence of genetic polymorphisms among the genes under study. 4) To explore whether any associations between the genetic polymorphisms in the genes under study confers any additional risk of prostate cancer occurrence and/or mortality.

This training award will allow the applicant to collect samples and perform genetic analysis for the APOJ/CLI gene. The applicant will be able to assess the feasibility of subject accrual and specimen collection in these minority populations. The prevalence of the genetic polymorphisms of interest in the targeted populations will be determined. With this information, appropriate sample sizes and power analyses can be carried out to plan a large study to assess the **a priori** hypothesis that the racial disparities in prostate cancer risk and mortality are due to genetic environmental interactions. Understanding the basis for the adverse prostate cancer risks faced by African-American men could lead to interventions including behavioral modifications, nutritional supplements, or therapies.

The applicant's access to African American subjects as well as his access to a large immigrant population made up of Caribbean blacks and non-white Hispanics provides a significant opportunity to conduct this study. Moreover, utilization of the applicant's international contacts will ensure the incorporation of continental African men as well as Caribbean men for study analysis at a future time.

This training award will enable the applicant to establish the pilot data necessary to pursue a ROI or related grant. The applicant will continue to foster his primary collaborative relationships while developing others. Most importantly, this training award will provide the applicant with a considerable opportunity to further his endeavors to become an independent investigator in the fight against prostate cancer.

Proposal Body

Collaborative Arrangements: Alfred I. Neugut, M.D., and Ralph E. Buttyan, Ph.D served as my collaborators in the DOD training award (MP980014). In this training plan, I will continue a direct working relationship with both Alfred I. Neugut, M.D., Ph.D. and Ralph E. Buttyan, Ph.D. Dr. Neugut holds a joint position as an Associate Professor in Medicine: Oncology Division, and the School of Public Health at Columbia University. Dr. Neugut has vast experience in both clinical and epidemiologic research in breast and colon cancer, and is currently conducting a study in prostate cancer to define the role of alternative therapies among patients with prostate cancer. My relationship with Dr. Neugut has been very instructive. Moreover, Dr. Neugut has assisted in the planning and design of the present study.

Dr. Buttyan is an Associate Professor of Pathology and Urology and is Director of the Molecular Urology Laboratory at Columbia University and he will continue to serve as a mentor for Dr. Franklin in his organization of this research project. Dr. Buttyan has extensive experience in the molecular biology of prostate cancer as attested to by his attached bibliography. As well, his laboratory has extensive experience with the PCR techniques needed in this project and his laboratory contains a full repertoire of equipment that will be needed for these studies. There are three senior staff members (Ph.D) and two technical assistants in the laboratory, some of who will be able to assist in the development of the techniques needed here.

Career Development: The applicant's pursuit of a career in academic medicine included a two-year Fellowship in Urologic Oncology and ongoing studies towards a MPH degree in Epidemiology. Throughout the applicant's residency and fellowship training, he has been engaged in both clinical and basic research in prostate cancer. Augmenting these clinical and basic research experiences with his training in epidemiology is a primary focus of the applicant. Prostate cancer is a major disease and its impact on the American population is expected to escalate as the population ages. Despite the vast body of research in this disease entity, the field is littered with many unanswered questions. Solutions to many of these questions such as the evaluation of differences in prostate cancer risk and mortality between blacks and whites will be facilitated by the application of epidemiologic principles. The applicant requests 25% support from the proposed training grant, and he expects a matching commitment in terms of institutional support for a total of 40 percent. During the course of this project the applicant will collect the blood specimens from study subjects. Specifically for this training award, the applicant will proceed by processing and analyzing samples for the genetic polymorphisms in the APOJ/clusterin gene. This will allow the applicant to enhance his technical skills in PCR technology and DNA analysis. The applicant will continue to work on establishing his major relationships both locally and internationally. Pilot data derived from this project will serve as the foundation for a large scale RO1 or other type of grant funding. These milestones will serve to establish the applicant as an independent prostate cancer investigator.

Applicant's Research Background, Current Program of Research and Future Goals:

The applicant has been engaged in both basic and clinical research:

During the applicant's residency training at Columbia University, he worked on the development of a cDNA library derived from the rat prostate gland.

The applicant participated in a project to identify and characterize prostate specific Homeobox genes. The applicant performed in vitro and in vivo experiments to evaluate the efficacy and specificity of viral gene constructs encoding a novel prostate specific antigen (PSA) promoter and the luciferase marker gene. The applicant was a co-investigator and contributed to the development of a grant proposal to assess the ethnic/racial variations in access and utilization of health care by veterans.

The applicant has a tract record of recruiting subjects into clinical trials as exemplified by the following: He served as the principal investigator for 2 clinical trials utilizing Liarozole in the treatment patients with prostate cancer manifesting early (PSA) failure after primary therapy as well as in patients with initial hormone failure.

He is the principal investigator for a recently submitted "National phase II trial of Intron, interferon alfa 2b plus BCG for superficial bladder cancer."

The applicant's is a recent recipient of a DOD Minority Population Focused Training Award (MP980014). Associated with the DOD training award MP980014, an IRB proposal for this award is pending. The applicant has also established commitments from the following persons to contribute subjects for the study: Ron Inis, M.D., Columbia University, Department of Radiation Oncology. Daniel Petrylak, M.D., Columbia University, Department of Medicine (Oncology Division). Gerald P. Hoke, M.D., Director of Urology, Harlem Hospital. Errol Mallet, M.D., Community Urologist, Brooklyn. On the international front, the applicant has acquired a commitment from Alex Danso, M.D., Ph.D., Zimbabwe, and A verbal commitment from Lawson Douglas, M.D., Jamaica WI.

During his fellowship training at UCLA School of Medicine, the applicant contributed to the development of data bases utilizing patients with prostate cancer and kidney cancer. These databases continue to serve as the foundation of many research projects.

The applicant is nearing completion of a MPH in epidemiology at the Joseph Mailman School of Public Health, Columbia University.

The goal of the applicant is to merge his urologic, epidemiologic, and basic research experiences into the domain of molecular epidemiology, and establish himself as an independent investigator in prostate cancer research.

The goal of the applicant is to develop his career in academic medicine to teach and serve as a mentor to others.

Study Purpose and Rationale

Specific aims: 1) To determine whether certain genetic variations in the androgen receptor gene, the vitamin D receptor gene, SRD5A2 gene, the CYP3A4 gene, or the apolipoprotein-J/clusterin gene distinguish African American populations from other ethnic varieties. 2) To assess whether the occurrence of particular genetic variations in any of these five genes might correspond to a higher risk for prostate cancer occurrence and mortality in the African American population. 3) To evaluate if there is any relationship in the occurrence of genetic polymorphisms among the genes under study. 4) To explore whether any associations between the genetic polymorphisms in the genes under study confers any additional risk of prostate cancer occurrence and/or mortality.

Background and Rationale

Prostate cancer risk is approximately 50% more common among African American men than white men (1). At the same time, prostate cancer has twice the mortality rate among African American men as among white men (1). Variations in access and utilization of health care do not completely account for these differences (2). Emerging evidence also suggests that the increased risk of prostate cancer observed among African Americans may, in fact, extend more generally to African blacks (3). This is supported by recent studies demonstrating a high incidence rate of prostate cancer among Jamaicans and new data from the African continent suggesting a higher than expected prostate cancer incidence rate among Africans on the continent (4,5). Whether the observed risk among blacks is primarily genetic in origin, environmental, or is derived from a genetic interaction with environmental factors such as a high fat diet is not known. Several hot spots for genetic variation to identify the basis for this prostate cancer disparity have been investigated. Among these, the vitamin D receptor and the androgen receptor have already shown promise. Genetic variability has been observed between white and black Americans in the frequency with which certain genetic polymorphisms can be detected in the androgen receptor (AR) gene and the vitamin D receptor (VDR) gene (6-8). While the AR gene product plays a pivotal role in the regulation of prostate cellular growth, the VDR gene product has shown antiproliferative and prodifferentiation responses in prostate cancer cell lines. It has been observed that CAG and GGC repeat lengths in the androgen receptor have inverse relationships with the transcriptional activity of this receptor. Shorter CAG and GGC repeat lengths are associated with higher transcriptional activity. The prevalence of short CAG repeats (< 20) in African American men was estimated to be about 75%, compared to 62% in non-Hispanic whites, and 49%

in Asians. Similarly, shorter GGC allele lengths (<16) have been found in higher frequencies in African Americans as compared to whites and Asians. It is believed that the increased prevalence of short CAG/GGC repeat lengths may contribute to the higher incidence and mortality rates of prostate cancer observed among African Americans. Within the VDR gene, polymorphisms in the poly-A microsatellite region at the 3' untranslated domain (3'UTR) were associated with prostate cancer occurrence among white males. Men with long (L) alleles (A18 to A22) were observed to have a 4.25-4.52 higher risk when compared to men with short (S) alleles (A14-A17). Furthermore there appears to be an association between L alleles and advanced prostate cancer. Although an analysis of the VDR poly-A microsatellite region in black men revealed no association with either prostate cancer risk or tumor stage, polymorphisms in the BsmI restriction site, in conjunction with the poly-A microsatellite, was observed to be associated with an increased risk of prostate cancer. The B type BsmI restriction site combined with a long poly-A microsatellite was observed to be associated with an increased risk of prostate cancer in African American men. In contrast, the b type BsmI and the L allele were associated with decreased risk. No association with prostate cancer was observed for BsmI (B or b) linkages with S alleles. These finding were different from those observed among white men where the BsmI restriction site could be used interchangeably with the poly-A microsatelite to determine prostate cancer risk.

Genetic polymorphisms have also been identified among blacks and whites in the apolipoprotein-J/clusterin gene (9-13). Intriguingly, the protein product of the apolipoprotein-J/clusterin (APOJ/CLI) gene is associated with programmed cell death observed when prostate cancer cells undergo apoptosis following androgen withdrawal. Although there was extensive speculation that the clusterin protein might be a suicide gene activated in response to apoptotic stimuli, more recent studies suggest, in fact, that this product is induced in apoptotic cells as a means of attempting to protect the cell against noxious stimuli. Indeed more recent evidence shows that prostate cancer cells that overexpress clusterin are more protected against cell death stimuli (Chung Lee, and associates). Polymorphisms in the APOJ/CLI gene appear to be predominant in 2 populations of African ancestry (African Americans and Nigerian blacks). Finally, it should be noted that this gene is located within a chromosomal site (8p22-24) that is frequently found to be altered in prostate cancer. No study, to date, has reported on the variability of genetic polymorphism of the apolipoprotein-J/clusterin gene and differences in prostate cancer risk between blacks and whites.

Two other candidate prostate cancer genes (the 5α-reductase type II gene, and the CYP3A4 gene) involved in androgen metabolism have also shown promise (14, 17). The 5α-reductase type II (SRD5A2) gene coverts testosterone to dihydrotestorone (DHT), which is the most active physiologic steroid in prostate growth and development. Polymorphisms in this gene have been identified as variations in the length of TA dinucleotide repeats. Ethnic variability in the polymorphisms of the SRD5A2 gene has been identified. Longer TA dinucleotide repeat lengths were observed at a higher frequency among African Americans than other ethnic groups studied (14). In a case control study performed on a predominantly white male population, long TA dinucleotide repeats were observed less frequently among prostate cancer cases than among the controls (15). This observation suggests that, at least among whites, long TA repeats is not associated with higher prostate cancer risk. The CYP3A4 gene is a member of the cytochrome p450 supergene family and is involved in testosterone oxidation (16). Rebbeck et al. have shown that a variant CYP3A4 gene (CYP3A4-V) is associated with higher stage (T3/T4) prostate cancers in older men (age > 63 years) (17). Their findings may help explain the inter-individual variability of the Cyp3a4 protein observed in another study (18). To date no study has been performed to determine if ethnic cultural variability exists in the CYP3A4 gene, and whether any detected variability could help explain the observed differences in prostate cancer risk and mortality among blacks and whites.

The growing evidence (discussed above) supports a premise for a genetic explanation of the differences observed in prostate cancer risk and mortality between whites and blacks. The Goals of this study are to further evaluate the relationship of these genetic polymorphisms with prostate cancer in different ethnic/racial groups.

Methods

<u>Subjects</u>: Subjects will consist of adult men age 50 years and above. Subjects will be classified as cases if they have a diagnosis of prostate cancer, and will be classified as controls if they do not. We will recruit a sample of 50 cases and 50 controls from each of the following populations: whites, black Americans, black Caribbean, non-white Hispanics. Recruitment from these populations will be focussed around the New York Presbyterian Hospital, which serves a large ethnically diverse population. Because we expect under-recruiting of black American and black Caribbean cases at the New York Presbyterian site efforts will be made to obtain patients from doctors private offices in Harlem, Brooklyn and Queens.

Subjects will be recruited into the study from several sources. The New York Presbyterian Hospital Urology centers at the Atchley Pavilion and the Allen Pavilion. These 2 locations represent the largest source of patients to the New York Presbyterian Hospital's urology services. The Allen Pavilion was incorporated into Columbia Presbyterian Medical Center with the primary mission of delivering community-based medical care to the Washington Heights and Inglewood communities of Manhattan, New York. These communities are largely made up of persons of non-white Hispanic origins. Thus the Allen pavilion will represent the main access to the non-white Hispanic population. The Department of Radiation Oncology at the New York Presbyterian Hospital will also serve as a primary location for subject recruitment. Doctors private offices in Brooklyn, Manhattan, and Queens will serve as venues for the recruitment of black American and black Caribbean subjects. After signing an informed consent, subjects will be requested to complete a questionnaire and provide a small blood sample.

Source of DNA: DNA for analysis will be obtained from blood. Each subject will be required to sign an informed consent and complete a questionnaire before enrollment into the study. A specimen of blood will be obtained from each subject. This blood will be taken to the laboratory where it will be processed for DNA extraction.

Genotyping of DNA Polymorphism

Analysis of CAG and GGC repeat lengths: The following PCR amplification technique will be utilized to evaluate the androgen receptor CAG repeat polymorphism. DNA extracted from blood using standard techniques will serve as the template. ³²P labeled oligonucleotides bordering the CAG repeat on either side will be synthesized in order to facilitate its amplification. Similarly, ³²P oligonucleotides bordering the GGC repeat on either side will be synthesized to promote the amplification of this repeat. CAG repeat lengths and GGC repeat lengths will be amplified separately using their respective bordering oligonucleotides. The PCR products will be isolated using electophoresis on a polyacrylamide gel and autoradiographed. Repeat lengths will be determined by applying direct sequencing of the PCR product.

Analysis of Vit D receptor gene: Amplification of the VDR 3'UTR poly-A microsatellite will be accomplished using the approach described by Ingles et al. (6). An unlabelled primer (5'-GTGTAGTGAAAAGGACACCGGA-3') and one $[\gamma^{-33}P]$ adenosine triphosphate end labeled primer (5'-GACAGAGGAGGGCGTGACTC-3') will be synthesized and utilized for the PCR amplification. PCR products will be separated on polyacrylamide sequencing gels and autoradiographed. Allele sizes will be scored by comparison with known control sizes.

BsmI restriction fragment length polymorphism will be analyzed using the method described by Morrison (20). The DNA region containing the BsmI polymormphic site in intron 8 will be amplified. DNA cleavage utilizing BsmI restriction enzyme will be performed and the DNA products electrophoresed on a polyacrylamide gel. The BsmI b allele, which represents presence of the site, will be identified by the production of 2 bands (21)

Analysis of APOJ/CLI gene

Amplification of the APOJ-coding exon 7 will be accomplished by utilizing PCR primers, which flank this region as described by Tycko et al. (12). The PCR product will be separated using a 6% acrylamide gel then subjected to direct sequencing. The APOJ exon 7 polymorphisms will be characterized as JVIIA, JVIIB and JVIIC as was defined by Tycko et al. The JVIIB allele has an A to C replacement at nucleotide position 1025, which corresponds to a substitution of histidine for asparagine at amino acid position 317. The JVIIC allele has a G to A replacement at nucleotide position 1058, which corresponds to a substitution of asparagine for aspartate at amino acid position 328.

Analysis of the CYP3A4 gene

We will perform an analysis of the CYP3A4 gene by amplifying a 592 bp fragment upstream of the coding region of CYP3A4 gene utilizing flanking primers as described by Rebbeck et al. PCR products will be tested and characterized as homozygous wild-type (w/w), homozygous variant (v/v), or heterozygous (w/v) by electorophoresing 2 samples from each individual on a polyacrylamide gel. PCR-generated homozygous variant from a known +v/v subject will be placed in one of the wells. A change in the band pattern is expected only when the known v/v DNA is added to w/w products. Direct sequencing will be carried out on the v/v and w/v products to confirm the A to G nucleotide transition mutation in the nifedipine-specific element located at -287 to -297 bp from the transcription start site of the CYP3A4 gene (17).

Statistical Analysis

The aim of this study is to investigate the relationship between the length of a polymorphic CAG repeat sequence occurring in the androgen receptor gene, the presence of variations in the ApoJ/clusterin and the vitamin D receptor gene in subjects with and without prostate cancer in different ethnic groups. We will use logistic regression to estimate adjusted odds ratios of developing prostate cancer for different CAG repeat sequences, and presence or absence of genetic variations on the vitamin D gene and the ApoJVIIB allele while controlling for other prognostic factors. We expect that shorter CAG repeat sequences, and variations on the Apoj/clusterin gene and the vitamin D receptor gene will be associated with higher likelihood of prostate cancer and that ethnic groups who present with higher prevalence of these variations will be at higher risk of development of prostate cancer.

For power calculation purposes we will use the prevalence of patients with CAG repeats less than or equal to 22. In a study by Irvine et al. the prevalence of subjects with CAG repeats less than or equal to 22 is approximately 70% with some variability among the different ethnic groups (75% for African Americans, 62% for whites). The prevalence of variations in the vitamin D receptor gene and the JVIIB variant of the APOJ gene vary from 0% to 30% across the different ethnic groups (for the JVIIB variant the prevalence is 28% in Blacks and 0% in whites; for the vitamin D receptor gene the prevalence of the BL combination is 3%, 10% and 21% in whites, Hispanics and Blacks, respectively).

We will sample 50 cases of prostate cancer and 50 controls for each ethnic group for a total of 300 subjects. The tables below give the power of the Fisher exact test comparing prostate cancer rates for a range of CAG repeats <= 22 and variations in the ApoJ and the vitamin D receptor genes prevalences and ratios for prostate cancer free rates. For example, from table 1 we read that if the prevalence of patients with CAG repeats less than or equal to 22 is 70% and men with the shorter CAG repeats have a prostate cancer rate 2.5 times the rate of men with longer CAG repeats the power of our test will be 90%. From table 2 we read that if the prevalence of patients with variations in the ApoJ or the vitamin D receptor gene is 15% and men without the variations have a prostate cancer rate 0.3 times the rate of men with the variations the power of our test will be 75%.

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Table 1. Power for detecting differences by CAG repeats less than 22

	odds R	latios	
2.0	2.5	3.0	3.5
0.83	0.97	1.00	1.00
0.78	0.95	0.99	1.00
0.50	0.72	0.85	0.92
	2.0 0.83 0.78 0.71 0.62	2.0 2.5 0.83 0.97 0.78 0.95 0.71 0.90 0.62 0.83	Odds Ratios 2.0 2.5 3.0 0.83 0.97 1.00 0.78 0.95 0.99 0.71 0.90 0.97 0.62 0.83 0.93 0.50 0.72 0.85

Table 2. Power for detecting differences by ApoJ2 and BL

Prev-	Odds Ratios
alence	0.20 0.25 0.30 0.35 0.40 0.45 0.50
0.10	0.67.0.56.0.47.0.28.0.21.0.25.0.20
0.15	0.67 0.56 0.47 0.38 0.31 0.25 0.20 0.92 0.85 0.75 0.65 0.54 0.45 0.36
0.20	0.99 0.96 0.90 0.82 0.72 0.61 0.50
0.25	1.00 0.99 0.96 0.91 0.83 0.73 0.62
0.30	1.00 1.00 0.99 0.96 0.90 0.82 0.71
0.35	1.00 1.00 0.99 0.96 0.90 0.82 0.71 1.00 1.00 1.00 0.98 0.95 0.88 0.78

Statistical analysis will be performed by Emelia Bagiella, Division of Biostatistics, School of Public Health.

Future Directions

The applicant will be able to assess the feasibility of subject accrual and specimen collection in these minority populations. The prevalence of genetic polymorphisms of interest in the targeted populations will be determined. With this information, appropriate sample sizes and power analyses can be carried out to plan a large-scale study to assess the **a priori** hypothesis that the racial disparities in prostate cancer risk and mortality are due to genetic environmental interactions. Understanding the basis for the adverse prostate cancer risks faced by African-American men could lead to interventions including behavioral modifications, nutritional supplements, or therapies.

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2.c. BIOGRAPHICAL SKETCH

Applicants should include this form as Addendum B in the submitted proposal.

Provide the following information for the applicant and collaborating investigator listed on the detailed cost estimate

Name	POSITION TITLE
John Roland Franklin, M.D.	Assistant Professor of Urology
EDUCATION/TRADIDIC (Pagin with based assets as at a fairle of	

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)

. Institution and Location	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
Queens College, New York Queens College, New York Columbia University, New York UCLASchool of Public Health, L.A., CA (9/96 - 6/97.) Columbia School of Public Health, N.Y.(9/97 - present)	B.A. M.A. M.D. M.P.H. Expected	1984 1984 1988 Degree Expected Fall, 1999	Chemistry Chemistry Medicine Epidemiology Epidemiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds 2 pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

1988 - 1989	Intern, Nassau County Medical Center, East Meadow, NY
	Urology Research, Columbia University, NY
<u> 1990 - 1994</u>	Urology Residency, Columbia Presbyterian Medical Center, NY
1994 - 1995	Clinical Urolgic Oncology Fellow, UCLA School of Medicine, CA
	Research Urologic Oncology Fellow, UCLA School of Medicine, CA
	Staff Urologist, West L.A. VAMC, CA
1996 - 1997	Assistant Clinical Professor, UCLA School of Medicine, CA
	Co-Chairman, Prostate Cancer Center of Excellence, West L.A.
	VAMC, CA
1997 - 1998	Assistant Professor of Urology, Albert Einstein College of
	Medicine, Bronx, NY
March 1998 - Present (Columbia University, Assistant Professor of Urology
March 1998 - Present F	Presbyterian Hospital, Assistant Attending

PROFESSIONAL ACTIVITIES AND HONORS: American Urologic Association, National Medical Association, Columbia University College of Physician and Surgeons Alumni, Oueens College Alumni, Peer Reviewer, The Journal of Urology, UCLA's Department of Epidemiology, School of Public Health Traineeship Award - 1996, National Institute of Health, Tumor Immunology Training Grant - June 1995, American Foundation for Urologic Disease, Inc., National Kidney Foundation Joint Resident Fellowships - 1992, First Prize Essay Contest Winner - The Society of Basic Urologic Research - 1992, Salk Scholar Award - 1984, Queens College Graduate Student Award - 1984, Queens College Division of Mathematics and the Natural Sciences Award - Honors in Chemistry - 1984

REFERENCES:

Franklin JR, Olsson CA, and Sawczuk IS. Safety of Urologic Surgical Interventions in the Elderly. Geriatric Nephrol. and Urol. 2: 105 (1992).

Franklin J, and Benson M. New Techniques in Management and Treatment of Superficial Bladder Cancer. In DE Neal (ed.), Tumours in Urology. Springer-Verlag London Berlin Heidelberg New York, pp 65-78 (1994).

Franklin JR, and deKernion JB. Surgical Approaches To Renal Cell Carcinoma. in MS Ernstoff et al. (ed), Urologic Cancer. W.W. Norton & Company, N.Y., London (1996).

Belldegrun A, Franklin JR, Figlin R: Prognostic factors in renal cell carcinoma. J Urol. 154:1274 (1995).

Franklin JR, deKernion JB: Kidney tumors - what's new? Current Opinions in Urology 5 (5):225 (1995).

Franklin JR, Raz S, deKernion JB: Female neobladder construction utilizing the UCLA 1 (ileocolic) pouch. In Olsson CA (ed), Surgical Techniques in Urology. 8 (5) (1995).

Franklin JR, Figlin R, Belldegrun AS: Renal cell carcinoma: Basic biology and clinical behavior. Seminars in Urologic Oncology 14 (4):208 (1996).

Franklin JR, Figlin R, Rauch J, Gitlitz B, Dorey F, deKernion JB, and Belldegrun AS: The role of cytoreductive surgery in the management of metastatic renal cell carcinoma. Seminars in Urologic Oncology 14 (4):230 (1996).

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Patel A, Dorey F, Franklin J, and deKernion J: Recurrence patterns after radical retropubic prostatectomy: Clinical utility of PSA doubling times and log slope PSA (prostate specific antigen). J Urol., 158: 1441-1445, 1997.

Hoh C, Spencer MA, Franklin J, deKernion JB, Phelps ME, Belldegrun A: Positron emission tomography in urologic oncology. J Urol, 159: 347-356, 1997.

Belldegrun AS, Franklin JR, O'Donnell MA, Gomella LG, Klein E, Neir R, Nseyo UO, Ratliff TL, Williams RD: Superficial Bladder Cancer: The role of Interferon-alpha. J Urol., 159: 1793-1801, 1998.

Figlin R, Gitlitz B, Franklin J, Dorey F, Moldawer N, Rausch J, deKernion J, and Belldegrun A: Interleukin-2-based immunotherapy for the treatment of metastatic renal cell carcinoma: an analysis of 203 consecutively treated patients. Cancer J Scientific Amer., 3(suppl 1): 92-97, 1997.

MANUSCRIPTS IN PREPARATION:

. •

Franklin JR, Dorey J, Patel A, Litwin MS, deKernion J: Improved continence after radical retropbic prostatectomy: A modified apical dissection.

Franklin JR, Werthman P, Aronson W, Dorey F, Smith R, Rajfer J, and deKernion J: Peyronie's disease occurring after radical prostatectomy: Fact or friction?

PRESENTATIONS AT PROFESSIONAL MEETINGS PUBLISHED AS ABSTRACTS:

Franklin JR, and Bittman R, Ph.D. Synthesis of the alkyl ether phospholipid, racglycerol-3-phosphorylcholine 1-dodecyl ether 2-eicosyl ether and 1-eicosyl ether 2-dodecyl ether. 17th marm Abstract Booklet (ACS, April 1983) p. 208.

Franklin, J: The novel expression of homeobox genes in the mammalian prostate. Ferdinand C. Valentine Urology Residents' Essay Meeting. (The New York Section of the AUA, Inc., April 1992) Abstract 74.

Franklin JR, Olsson CA, and Buttyan R. Expression of homeobox genes in the rat ventral prostate gland. J Urol 147: 318A (1992)

Franklin JR, Olsson CA, and Buttyan R. Homeobox gene expression in the mammalian prostate gland. Pan African Urological Surgeons Association (Inaugural international conference). Harare, Zimbabwe, May 1992.

Franklin, JR, and Hensle, T: Conservative management of renal pelvic lesions inchildren. Pan African Urological Surgeons Association (Inaugural international conference). Harare, Zimbabwe, May 1992.

Barbara GJ, Franklin JR, Figlin, RA, William P, deKernion J, Belldegrun A: Tumor infiltrating lymphocyte (TIL) based therapy for metastatic renal cell carcinoma (RCC). The UCLA Kidney Cancer Program. National Medical Association (Centennial Meeting). July 30, 1995.

Sokoloff M, Tso C-L, Kaboo R, Franklin J, deKernion J, Pang S, Figlin R, and Belldegrun A: Improved prostate cancer (PC) staging using supersensitive and quantitative polymerase chain reaction (PCR). Western Section American Urological Association (71st Annual Meeting). (Abs. 51) Nov 5-9, 1995.

Franklin JR, and deKernion JB: Radiation therapy for localized recurrence after radical retropubic prostatectomy. Western Section American Urological Association (71st Annual Meeting). (Abs. 233) Nov 5-9, 1995.

deKernion JB, Trapasso JG, Franklin JR: Improved continence following radical retropubic prostatectomy: a modified apical dissection. Western Section American Urological Association (71st Annual Meeting). (Abs. 78) Nov 5-9, 1995.

Franklin JR, Raz S, and deKernion JB: Ileocolonic female neobladder. Western Section American Urological Association (71st Annual Meeting). (Abs. 168) Nov 5-9, 1995.

deKernion J. Raz S. Franklin J. and Seto E: Long-term results of the continent ileocecal urinary reservoir. Pan African Urological Surgeons' Association (2nd Biennial Conference) Sept 4-8, 1995.

deKernion J, and Franklin J: Improved preservation of continence after radical prostatectomy or cystectomy. Pan African Urological Surgeons' Association (2nd Biennial Conference) Sept 4-8, 1995.

Sokoloff M, Tso C-L, Randhir K, Franklin J, deKernion J, Pang S, Belldegrun A: Super-sensitive and quantitative polymerase chain reaction (PCR): An innovative technique for staging and monitoring prostate cancer. J Urol 153:294A, 1995.

Franklin J, Hoh C, Gitlitz B, Phelps M, Figlin R, and Belldegrun A: Positron emission tomography (PET) scan for imaging of advanced renal cell carcinoma (RCC). Proceeding of the American Urologic Association. J Urol., 155(suppl): 581A, 1996.

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Dorey F, Franklin J, deKernion J, and Smith R: Use of multiple PSA values for predicting clinical disease recurrence after radical retropubic prostatectomy (RRP). Proceeding of the American Urologic Association. J Urol., 155(suppl): 487A, 1996.

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Sokoloff M, Tso C-L, Franklin J, Nelson S, Dorey F, deKernion J, and Belldegrun A: Quantitative polymerase chain reaction [PCR] does not improve prostate cancer [PC] staging: A clinical-pathologic-molecular analysis of 121 patients. Proceeding of the American Urologic Association. J Urol., 155(suppl): 417A, 1996.

Belldegrun A, Franklin J, Dorey F, Rauch J, deKernion J, and Figlin R: Long termsurvival of 181 patients with metastatic renal cell carcinoma (mRCC) treated with IL-2 based immunotherapy with/without tumor infiltrating lymphocytes. Proceeding of the American Urologic Association. J Urol., 155(suppl): 385A, 1996.

Franklin J, Marks L, Dorey F, Shery ED, and deKernion J: Serum PSA levels following TURP in men with BPH: Long-term characterization. Proceeding of the American Urologic Association. J Urol., 155(suppl): 378A, 1996.

Hoh CK, Figlin RA, Belldegrun A, Moon DH, Franklin J, Phelps ME, and Maddahi J: Evaluation of renal cell carcinoma with whole body FDG PET. Proceeding of the 43rd annual meeting of the society of nuclear medicine. J Nuclear Med., 37(suppl): 141P, 1996

Franklin JR, deKernion JB, Patel A, Smith RB, Dorey F, and Rajfer J: Peyronie's disease occurring after radical retropubic prostatectomy: Fact or friction. Western Section American Urological Association (72nd Annual Meeting). (Abs. 166) Jul 28 - Aug 1, 1996.

Franklin J, Dorey F, Gitlitz B, deKernion J, Figlin R, and Belldegrun A: The role of combination surgery and immunotherapy in the management of advanced renal cell carcinoma. Western Section American Urological Association (72nd Annual Meeting). (Abs. 110) Jul 28 - Aug 1, 1996.

Belldegrun A, Franklin J, Dorey F, Gitlitz B, Rauch J, deKernion J, Figlin R: Patients with metastatic cell carcinoma (mRCC) treated with IL-2 based immunotherapy with or without tumor infiltrating lymphocytes: Long term survival. Western Section American Urological Association (72nd Annual Meeting). (Abs. 109) Jul 28 - Aug 1, 1996.

deKernion JB, Franklin J, and Patel A: Radical retropubic prostatectomy: Improved continence after a modified apical dissection. Western Section American Urological Association (72nd Annual Meeting). (Abs. 3) Jul 28 - Aug 1, 1996.

Franklin J, Pang S, Dannul J, Sawyer C, Kaboo R, Tso C-L, and Belldegrun A: Cloning of an upstream regulatory region augments prostate specific antigen (PSA) promoter activity: In vivo studies. (Abstract) accepted AUA, April, 1997.

Belldegrun A, Franklin J, Dorey F, Rauch J, deKernion J, and Figlin R: Immunotherapy for renal cell carcinoma: The UCLA experience. (Abstract) accepted AUA, April, 1997.

Seltzer M, Hoh C, Franklin J, Naitoh J, Gitlitz B, Figlin R, Silverman D, deKernion J, Phelps M, Belldegrun A: Positron emission tomography (PET) imaging for staging of renal, testicular, and prostatic neoplasms. (Abstract) accepted AUA, April, 1997.

Naitoh J, Franklin J, Patel A, and deKernion J: Comparing results of patient-based and physician-based reported rates of urinary incontinence following radical prostatectomy. (Abstract) accepted AUA, April, 1997.

Hoh CK, Figlin RA, Seltzer MA, Belldegrun A, Franklin J, Gitlitz B, Phelps ME, Maddahi J: Prognostic value of a whole body FDG PET vs conventional imaging for the evaluation of biologic therapy in renal cell carcinoma. (Abstract) The Society of Nuclear Medicine 44th Annual Meeting, June, 1997.

Franklin JR: Endoscopic treatment for papillary TCC of upper tract. National Medical Association. August 2-7, 1997.

Franklin JR, Pang S, Dannul J. Sawyer C, Kaboo R, Tso C-L, and Belldegrun A: An Upstream regulatory region augments prostate specific antigen (PSA) promoter activity: In vivo studies. National Medical Association. August 2-7, 1997.

Franklin JR, Dorey J, Patel A, Litwin MS, deKernion J: Improved continence after radical retropubic prostatectomy: A modified apical dissection. National Medical Association. August 2-7, 1997.

Biographical Sketches

Provide the following information for the key p	ersonnel listed on the budget	page for the initial b	udget period
NAME Ralph Buttyan, Ph.D.		ofessor Of Pathol	
EDUCATION/TRAINING (Begin with baccalaureate or other initial prof	fessional education, such as nursing,	and include post-doctoral	training.)
INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
University of Pittsburgh	BS	1974	Biophysics & Microbiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds 2 pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Ph.D.

1980

Virology

1981-1983	Postdoctoral Research Fellow, Dept. of Urology
	Columbia University, New York, NY
1985-1988	Associate Research Scientist, Dept. of Urology
	Columbia University, New York, NY
1988-1992	Assistant Professor of Urologic Biochemistry,
	Columbia University, New York, NY
1992-1993	Assistant Professor of Pathology in Urology
	Columbia University, New York, NY
1993-Present	Associate Professor of Pathology in Urology and Director, Molecular Urology
	Columbia University College of Physicians and Surgeons, New York, NY

Professional Activities and Honors: Edwin R. Beer Award, New York Academy of Medicine, 1988 Invited Lecturer: Gordon Conference Cell Death and Aging, 1992; Keystone Conference on Programmed Cell Death, 1992; Juan March Foundation Lecture, 1993; Australian Endocrine Society, 1994; Endocrine Society, 1997; Scientific Board, IDUN Pharmaceuticals, San Diego. Scientific Reviewer for NCI, NIDDK, DOD and VA, CaPCURE Research Award 1986, 1987. Editorial Board, *The Prostate*, *Mol. Cell. Biochem*.

Relevant Publications (from 114)

University of Chicago

Buttyan, R., Sawczuk, I.S., Benson, M.C., Siegal, J.D. and Olsson, C.A. (1987) Enhanced expression of the *c-myc* protooncogene in high-grade human prostate cancers. The Prostate 11: 327-337.

Buttyan, R., Zakeri, Z., Lockshin, R.A. and Wolgemuth, D. (1988) Cascade induction of *c-fos*, *c-myc* and heat shock 70K transcripts during regression of the rat ventral prostate gland. Mol. Endocrin. 2: 650-657.

Appendix D

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Connor, J., Sawczuk, I.S., Benson, M.C., Tomashefsky, P., O'Toole, K.M., Olsson, C.A. and <u>Buttyan, R.</u> (1988) Calcium channel antagonists delay regression of androgen-dependent tissues and supress the gene activity associated with cell death. The Prostate 13: 119-130.

Rennie, P., Bruchovsky, N., <u>Buttyan, R.</u>, Benson, M. and Cheng, H. (1988) Gene expression during the early phases of regression of the androgen-dependent Shionogi mouse mammary carcinoma. Cancer Research 48: 6309

Buttyan, R., Olsson, C.A., Pintar, J., Chang, C., Bandyk, M., Ng, P.-Y. and Sawczuk, I.S. (1989) Induction of the TRPM-2 gene in cells undergoing programmed death. Mol. Cell. Biol. 2: 3473-3481.

Katz, A.E., Benson, M.C., Wise, G.J., Olsson, C.A., Bandyk, M.G., Sawczuk, I.S., Tomashefsky, P. and Buttyan, R. (1989) Gene activity during the early phase of androgen-stimulated rat prostate regrowth. Cancer Res 49: 5889-5894.

Sensibar, J.A., Griswold, M.D., Sylvester, S.R., <u>Buttyan, R.</u>, Bardin, C.W., Cheng, C.Y., Dudek, S., and Lee C. (1991) Prostatic ductal systems in rats: Regional variation in. localization of an androgen-repressed gene product sulfated glycoprotein-2. Endocrinology <u>128</u>: 2091-2102.

Colombel, M., Olsson, C.A., Ng, P.-Y. and <u>Buttyan, R.</u> (1992) Hormone-regulated apoptosis results from reentry of differentiated prostate cells onto a defective cell cycle. *Cancer Res.* 52: 4313-4319.

Colombel, M., Symmans, F., Gil, S., O'Toole, K.M., Chopin, D., Benson, M.C., Olsson, C.A., Korsmeyer, S. Buttyan, R. (1993) Detection of the apoptosis-supressing oncoprotein, bcl-2 in hormone-refractory human prostate cancers. Am. J. Path. 143: 390-400.

Buttyan, R. and Slawin, K. 1993 Rodent models for targeted oncogenesis of the prostate gland. Cancer and Metastasis Reviews 12: 11-19.

Zhang, X., Colombel, M., Raffo, A. and <u>Buttyan. R.</u> (1994) Enhanced expression of p53 mRNA and protein in the regressing rat ventral prostate gland. *Biochem. Biophys. Res. Comm.*, 198: 1189-1194.

Katz, A.E., Olsson, C.A., Raffo, A.J., Cama, C., Perlman, H., Seaman, E., O'Toole, K.M., McMahon, D. Benson, M.C. and Buttyan, R. (1994) Molecular staging of prostate cancer with the use of an enhanced reverse transcriptase-PCR assay. *Urology* 43: 765-775.

Colombel, M. and <u>Buttyan, R.</u> (1995) The rat ventral prostate gland: Model for hormone-regulated apoptosis *Methods in Cell Biol.* **46**: 369-385.

Colombel, M.C., Radvanyi, F., Blanche, M., Abbou, C., Buttyan, R., Donehower, L.A., Chopin, D. and Thiery, J.P. (1995) Androgen suppressed apoptosis is modified in p53 deficient mice. Oncogene 10: 1269-1274.

Appendix D

- RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.
- Katz, A.E., deVries, G., Begg, M., Raffo, A., Cama, C., O'Toole, K., Buttyan, R., Benson, M.C. and Olsson, C.A.: (1995) Enhanced reverse transcriptase-polymerase chain reaction for prostate specific antigen as an indicator of true pathological stage in patients with prostate cancer. Cancer, 75:1642-1648.
- Raffo, A., Perlman, H., Chen, M.-W., Day, M. and <u>Buttyan, R.</u> (1995) Overexpression of bcl-2 protects prostate cancer cells from apoptosis *in vitro* and confers resistence to androgen deprivation *in vivo*. Cancer Research, 55: 4438-4445.
- Olsson, C.A., de Vries, G.M., Raffo, A.J., Benson, M.C., O'Toole, K., Cao, Y., <u>Buttyan, R.</u> and Katz, A.E. (1996) Preoperative reverse transcriptase polymerase chain reaction for prostate specific antigen predicts treatment failure following radical prostatectomy. J. Urol. 155: 1557-1562.
- Dorai, T., Olsson, C.A., Katz, A.E., and <u>Buttyan, R.</u> (1997) Development of a hammerhead ribozyme against bel-2: I. Preliminary evaluation of a potential gene therapeutic agent for hormone-refractory human prostate cancer. The Prostate 32: 246-258.
- Zhang, X, Chen, M.-W., Ng, A., Ng, P.-Y., Lee, C., Rubin, M., Olsson, C.A. and <u>Buttyan, R.</u> (1997) Abnormal prostate development in C3(1)-bcl-2 transgenic mice. The Prostate 32: 16-26.
- Shen, R., Dorai, T., Szabolcs, M., Katz, A.E., Olsson, C.A. and <u>Buttyan</u>, R. (1997) Transdifferentiation of cultured human prostate cancer cells to a neuroendocrine phenotype in a hormone-depleted medium. Urol. Oncol. 3: 67-75.
- Buttyan, R., Zhang, X., Dorai, T. and Olsson, C.A. (1997) Anti-apoptosis genes and the development of hormone-resistant prostate cancer. In: *The Prostate Gland, Basic and Clinical Aspects*, R. Naz (ed), CRC Press, Inc., New York, NY, pp. 201-218.
- Dorai, T., Goluboff, E., Olsson, C.A. and <u>Buttyan, R.</u> (1997) Development of a hammerhead ribozyme against bcl-2. II. Ribozyme treatment sensitizes hormone-resistant prostate cancer cells to apoptotic agents. Anticancer Research 17: 3307-3312.
- Shabsigh, A., Chang, D.T., Heitjan, D., Kiss, A., Olsson, C.A., Puchner, P. and <u>Buttyan R.</u> (1998) Rapid reduction in blood flow to the rat ventral prostate gland after castration: Preliminary evidence that androgens influence prostate size by regulating blood flow to the prostate gland and prostatic endothelial cell survival. Prostate, 36:201-206.
- Perlman, H.R., Zhang, X., Chen, M.-W., Walsh, K. and <u>Buttyan. R</u>. (1998) Differential expression of bax and bcl-2 in the rat ventral protate gland after castration: an elevated bax/bcl-2 ratio corresponds with the onset of prostate epithelial cell apoptosis. Cell Death & Diff. 6: 48-54.
- Buttyan, R., Shabsigh, A, Perlman, H. and Colombel, M.C. (1999) Regulation of apoptosis in the prostate gland by androgenic steroids. Trends Endocrin. Metabol. 10: 47-54.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.

Photocopy this page or follow this format for each person.

NAME

POSITION TITLE

Alfred I. Neugut, M.D., Ph.D.

Associate Professor of Medicine and Public Health

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGRFE (If applicable)	YEAR(s)	FIELD OF STUDY
Columbia University College of Physicians & Surgeons, NY Columbia University, NY Columbia University School of Public Health, NY	M.D.	1977	Medicine
	Ph.D.	1977	Pathobiology
	M.P.H.	1983	Epidemiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES**.

Professional	Experience

1977-1978	Intern, Bronx Municipal Hospital Center, Bronx, NY
1978-1980	Resident in Medicine, Bronx Municipal Hospital Center, Bronx, NY
1980-1981	Clinical Fellow in Medical Oncology, Memorial Sloan-Kettering Cancer Center, NY
1980-1981	Clinical Instructor in Medicine, Cornell University Medical College, NY
1981-1983	Visiting Fellow in Oncology/Hematology, Columbia-Presbyterian Medical Center, NY
1981-1983	Staff Associate in Public Health (Epidemiology), Columbia University, NY
1983-1985	Assistant Professor of Medicine, Columbia University, NY
1983-1991	Assistant Attending Physician, Presbyterian Hospital, NY
1985-1991	Assistant Professor of Medicine and Public Health (Epidemiology), Columbia University, NY
1989-1991	Deputy Director for Cancer Epidemiology and Prevention, Comprehensive Cancer Center Columbia University NY
1991-1998	Associate Professor of Clinical Medicine and Public Health (Epidemiology), Columbia University, NY
1989-	Co-Deputy Director for Cancer Control, Comprehensive Cancer Center, Columbia University, NY
1989-	Co-Director, Oncology Outpatient Unit, Presbyterian Hospital, NY
1991-	Head, Program on Cancer Prevention and Control, Herbert Irving Comprehensive Cancer Center
1993-	Associate Attending Physician, Harlem Hospital Center
1991-	Associate Professor of Medicine and Public Health (Epidemiology), Columbia University, NY

Honors, A wards and Other

Mellon Fellow in Epidemiology and Medicine, Columbia School of Public Health and Department of Medicine Presybterian Hospital 1981-1990.

Junior Faculty Fellow of the American Cancer Society, Columbia University, 1984-1986.

Secretary Treasurer, American Society of Preventive Oncology, 1994-present.

Abstract Review Committees for the American Society of Preventive Oncology, American Society of Clinical Oncology, and American Gastroenterology Association, 1996

Member NCI Cancer Control Program Review Group, 1996-1997

President-Elect, American Society of Preventive Oncology, 1998

Selected Publications (Out of 129)

Neugut Al and Pita S: The role of sigmoidoscopy in screening for colorectal cancer: A critical review. Gastroenterology 95:492-499, 1988.

Neugut AI, Robinson E, Nieves J, Murray T and Tsai W-Y: Poor survival of treatment related acute non-lymphocytic leukemia. JAMA 264:1006-1008, 1990.

Neugut AI, Murray TI, Lee WC and Robinson E. The association of breast cancer and colorectal cancer in men: An analysis of SEER Program data. Cancer 68:2069-2073, 1991.

Neugut Al, Murray Tl, Garbowski GC, Treat MR, Forde KA, Waye JD, Fenoglio-Preiser C. The association of asbestos exposure with colorectal adenomatous polyps and cancer. JNCI 83:1827-1828, 1991.

PHS 398 (Rev. 4/98)

(Form Page 6) Page

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Existing/Pending Support:

John Roland Franklin, M.D. Existing

MP980014 (J. Franklin)

10/1/98 - 3/31/99

25%

Minority Population Focused Training Award

\$49,840

To promote the development of a prostate cancer research concept that focuses on the higher rate of prostate cancer incidence and mortality in African-Americans.

MP980014 (R. Buttyan)

10/1/98 - 3/31/99

10%

Minority Population Focused Training Award

\$49,840

MP980014 (A. Neugut)

10/1/98 - 3/31/99

7%

Minority Population Focused Training Award

\$49,840

Other Support

Format

NEUGUT, A.I. ACTIVE

5T32-CA09529-11A1 (A. Neugut)

7/1/96-4/30/01

as needed

Cancer Epidemiology, Biostatistics,

and Environmental Sciences Training Grant

\$316,324

To foster research training in the biomedical and behavioral sciences, specifically in cancer epidemiology for predoctoral and post-doctoral trainees.

1U01 CA ES66572-01 (M. Gammon)

8/1/95-7/31/99

20%

Breast Cancer and the Environment on Long Island

\$716,324

To determine whether environmental contaminants increase the risk of breast cancer among women on Long Island.

NCI CA66882-01A2 (A. Neugut)

9/30/96-8/31/2001

15%

Breast Cancer Education in North Manhattan

\$162,000

To utilize academic detailing to approach and instruct primary care physicians practicing in the two target communities on breast cancer prevention, screening, and state-of-the-art treatment approaches.

P30-CA13696-25 (K. Antman)

7/1/97-6/30/99

20%

Cancer Center Support Grant Supplement - Lung

Cancer After Breast Cancer Radiotherapy

\$103,000

To compare risks for lung cancer in breast cancer survivors who received RT and those who did not and to assess the dose-response relationship of lung cancer risk with radiation exposure.

NIH/NCI RO3 (H. Ahsan)

10/1/97-10/31/03

As needed

NAT2 genetic polymorphisms and risk of

breast cancer

\$85,241

To examine the effect of NAT2 gene and its interaction with cigarette smoking on breast cancer among a sample of women (300 cases and 300 controls) participating in the LIBCSP.

Army BCRP DAMD17981-9050 (H. Ahsan)

8/1/98-8/31/00

5%

Cytochrome P450-17a polymorphism and

risk of invasive breast cancer

\$68,427

To examine the association between polymorphisms of CYP17 gene and breast cancer.

P30-CA13696-25 (K. Antman)

7/1/98-6/30/99

10%

Cancer Center Support Grant

\$1,793,629

To support cancer research within the different Comprehensive Cancer Center's Core facilities (Head, Cancer Prevention and Control)

American Cancer Society (V.Grann)

1/1/98-12/31/99

7.5%

Measurement of quality of life in BRCA1 and 2

positive women

\$109,906

To confirm and extend the findings of this time trade-off methology pilot study.

NYSDOH (A. Neugut)

7/1/98-6/30/99

As needed

Columbia University Healthy Women's

Partnership

\$138,361

To provide screening, follow-up and referral for uninsured and under insured women.

Robert Wood Johnson Foundation

Center or Tobacco Research (D. Sadowsky)

1/1/99 -6/30/01

10%

Addressing Tobacco in Managed Care:

Columbia/PruCare Dental Proposal

\$500,000

To determine whether an MCO sponsored tobacco related system can be created, facilitated and maintained within the dental office.

PENDING

R25 NIH (A. Neugut)

12/1/99-11/30/04

15%

Promoting Colon Cancer Screening Among

Urban Blacks and Hispanics

\$237,548

To utilize a standardized, multi-component, culturally sensitive intervention based on the PRECEDE/PROCEED model to educate primary care physicians practicing in North Manhattan regarding colorectal cancer prevention, etc.

NCI RFA-CA98-014 (C. Basch)

12/1/99-11/30/03

5%

Tailored Communications for Colorectal

Cancer Screening

\$42,649

To evaluate the efficacy of computer-assisted tailored educational intervention to promote colorectal cancer screening as recommended by the NCI and the US Public Health Service.

P98-028 (Magai)

9/1/99-8/31/03

10%

Psychosocial Deterrents To Breast Cancer

Screening

\$347,792

To examine racial differences especially within group differences in the African American community based on culture of origin in women's use of breast cancer screening, psychosocial deterrents to screening and among those with history of breast diseases.

PO1 CA32617-09A3 (S. Stellman)

12/1/99-11/31/00

5%

Tobacco Carcinogenesis: Exposure, Metabolism

And Smoking

\$155,281

To identify all cases of tobacco-related cancer diagnosed at Columbia during the time-frame of the study. This is part of a greater case-control study.

OVERLAP

Budgets will be adjusted appropriately in conjunction with NCI staff if overlaps occur.

OTHER SUPPORT (1/17/99)

Buttyan, Ralph

Active

CA70769-02, (Aaron E. Katz, M.D.)

8/1/96 - 7/31/00

10% Committment

NIH/NCI

\$123,238 (Direct Cost year 02)

The Molecular Staging of Prostate Cancer

The goals of this project involve the further development and testing of a clinical blood assay involving RT-PCR technology to correctly stage human prostate cancers. No Overlap with this Project.

No Identifying # (Mitchell C. Benson, M.D.)

7/1/96 -6/30/99

10% Committment

T.J. Martell Foundation

\$195,000 (Direct Cost Year 02)

Basic and Clinical Studies on Prostate Cancer

This project examines the genetic basis for the development of hormone-resistant prostate cancer. Human prostate cancer cells are being studied for their ability to transdifferentiate to a neuroendocrine-like cell and the role of bcl-2 gene expression is being evaluated in hormoneresistant tumors. No overlap with current project.

RO1 DK53965 (R. Levin, Albany College of Pharmacy)

(P.I. of Subcontract, R. Buttyan)

04/01/98 - 03/31/01 15% Committment

NIH/NIDDK

\$113,970 (Direct Cost Year 01)

Molecular Pathway to Bladder Dysfunction

Work on this project studies the rabbit model of partial bladder outlet obstruction to define the genetic components that regulate the onset of bladder hypertrophy and dysfunction. No overlap with this project.

PC970137 (R. Buttyan)

06/01/98 - 12/01/00 15% Committment

Department of Defense

\$103,013 (Direct Cost Year 01)

Role of Cadherin T6 in Therapeutic Resistance of Prostate Cancer

This project characterizes a novel human cadherin, T6, and its role in protecting prostate cancer cells from apoptosis. No overlap with current project.

Pending Applications

No Identifying # (Mitchell C. Benson, M.D.)

7/1/99 -6/30/00

10% Committment

T.J. Martell Foundation

Basic and Clinical Studies on Prostate Cancer

\$195,000 (Direct Costs)

This is a renewal application for continuing support to examine the genetic basis for the development of hormone-resistant prostate cancer. If funded, it will extend our current support from this source. No overlap with current proposal.

P50 DK54186-01A (Steven A. Kaplan, M.D.) N.I.H. (RFA DK-98-018) 09/01/99 - 08/31/04 **25% Committeent** \$511,659 (Direct Costs First Year)

Ischemia and Angiogenesis in Urologic Diseases

This is an application for the O'Brien Urologic Center grant that has 3 projects and 2 Cores. Dr. Buttyan is the Principal Investigator on Project 1 (Regulation of Prostate Blood Flow by Androgens) that essentially overlaps 100% with the current application as well as the Director of Core B (Histology and Tissue Processing Core) in the Center. If the O'Brien Center application receives a score sufficient for funding, the current application would be withdrawn.

RO1 DK56808-01 (Raph Buttyan, Ph.D.) N.I.H. (NIDDK) 01/01/00 - 12/31/04 **25% Committeent** \$133,342 (Direct Costs First Year)

Regulation of Prostate Blood Flow by Androgens

This application is in complete overlap with the project submitted in consideration for the O'Brien Urologic Center and has been submitted separately in case the O'Brien Urologic Center application is not funded.

Yi-Chen Cao

Active

CA70769-02, (Aaron E. Katz, M.D.) NIH/NCI 8/1/96 - 7/31/00 **50% Committment**

\$123,238 (Direct Cost year 02)

The Molecular Staging of Prostate Cancer

The goals of this project involve the further development and testing of a clinical blood assay involving RT-PCR technology to correctly stage human prostate cancers. No Overlap with this Project.

Pending

None

Facilities/Equipment Description:

Laboratory:

This project will be performed in the Molecular Urology Laboratory of the College of Physicians and Surgeons of Columbia University. This is a modem, 4,OW sq ft research facility on the 15' floor of the Black Building on the Health Science Campus of Columbia University (West 168" St.) New York City. The facility contains all the equipment that might be necessary for molecular biology and biochemistry research. There are separate rooms housing a radioactive work area, a small animal surgery suite, a darkroom, a cell culture room and two offices for research fellows and associates. 3 technicians and 3 Associate Research Scientists as well as one Visiting Scholar and a Graduate Student staff the laboratory. Equipment present includes low temperature freezers for tissue storage, high, medium and low speed centrifuges for tissue processing, a full range of electrophroresis equipment for protein and nucleic acid analysis, a vacuum speed-vac for lvophilization of biological specimens, two PCR-thermocycler devices, two laminar flow hoods for cell culture work, two CO.) incubators that are utilized extensively for other projects in the laboratory, two computers for data processing an 'd an ELIS.A plate reader for NIT7 assays. Tissue analysis instrumentation including a cryostat, a microtome for embedded tissues and a light and fluorescent microscope are present in the facilities. Laboratory Animal Care facilities are on the 18' and 19'h Floors of the Black Building. These facilities are recently renovated and equipped with the most modem laboratory animal care equipment available.

Clinical:

The Principal investigator will have access to his target populations through the resources available at the Columbia-Presbyterian Medical Center in New York. In specific, the Principal investigator will have access to a general urology clinic at the Allen Pavilion and a multi-disciplinary urology clinic the Atchley Pavilion. The Allen Pavilion, located in a large Hispanic community, was incorporated into Columbia-Presbyterian Medical Center to enhance the institution's services to this community. The Allen Pavilion will be primary resource access to the non-white Hispanic male population. The Principal investigator will have access to a large local population of geographically diverse men of African descent (African-American as well as African-Caribbean) through his contacts with Harlem Hospital and community urologists in Brooklyn.

Computer/Office:

The Principal Investigator has a separate office in the Allen Pavilion, and secretarial support.

Dr. Neugut is equipped with an IBM PC at 640KB of RAM and 40MB hard disk. There is also an IBM PC AT clone with 20 MB hard disc for word processing with several software options including SIR, EGRET and BMDP. Dr. Neugut is currently in the Department of Epidemiology, which is an 800-sq. ft. fully furnished office space. This space also houses the UMPAC office and Ms. Sheinfelo Goins' office.

We also have access to the Columbia University Center for Computing Activities with 2 IBM 4341's and 2 DEC 20's. Software includes SAS, SPSS and programs by the Biostatistics facility.

STATEMENT OF ELIGIBILITY
Applicant's Name: John Roland Franklin, M.D.
Title of Proposal: <u>Assessment of Genetic Variations among Different Ethnic/Racial Groups:</u> An Explanation of Ethnic/Racial Disparities in Prostate Cancer Risk and Mortality.
Applicant's Organization Name: Columbia University
Applicant's Organization Location: New York City, New York
Signature of Applicant: John Franklin MD 3/7/99 STATEMENT OF ELIGIBILITY
For the purposes of the Department of Defense Congressionally Directed Medical Research Program's Prostate Cancer Research Program Minority Population Focused Collaborative Training Award category as outlined in the Announcement, the applicant fulfills all of the following criteria:
 Holds a position of at least an Assistant Professor or equivalent; AND
Has access to appropriate research facilities;
I, <u>Carl A Olsson, M.D.</u> of <u>Columbia University</u> (printed name of Department Chair, Dean or equivalent official)(printed name of institution)
attest that the above-named investigator fulfills the requirements for a Minority Population
Focused Collaborative Training Award.
Signature of Official BAOLH Date 3/8/99







Department of Urology

College of Physicians and Surgeons of Columbia University

Carl A. Olsson, M.D. John K. Lattimer Professor and Chairman **Squier Urological Clinic**

The Presbyterian Hospital in the City of New York

Tel: (212) 305-0100 Fax: (212) 305-0106

February 4, 1999

Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (PCRP99-Announcement)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702

To Whom It May Concern:

The Department of Urology at the College of Physicians and Surgeons congratulates Dr. John Franklin on the receipt of his first Department of Defense Award. We remain totally dedicated to the career of Dr. John Franklin. Dr. Franklin is an assistant professor in our faculty, and he has demonstrated a strong commitment to research. He will be relieved of clinical and administrative responsibilities in order for him to pursue his academic career development in the research plan that he outlines.

Dr. Franklin is a Caribbean-American physician who spends much of his clinical and administrative time with the African-American community patients in New York City. He has established collaborative relationships with Ralph Buttyan, Ph.D. who is also a member of the Department of Urology at Columbia, as well as with Alfred Neugut, M.D., Ph.D. of our School of Public Health, an experienced epidemiologist.

In this proposal they will continue their efforts to assess the ethnic/racial variations of genetic polymorphisms in the following genes in men with prostate cancer: Vitamin D receptor gene, the androgen receptor gene, and APOJ/Clusterin gene. Additionally, they will begin to evaluate genetic polymorphisms in the CYP3A4 gene as well as the SDR5A2 gene. These genes are important in prostate cellular metabolism and are potential contributing factors in the adverse manifestation of prostate cancer in the African-American male population.

I enthusiastically support Dr. Franklin's application.

Very sincerely,

Carl A. Olsson, M.D.

Calles

Columbia School of Public Health



Division of Epidemiology

March 8, 1999

US Army Medical Research and Materiel Command Attn: MCMR-PLF (PCRP99) 524 Palacky street Fort Detrick, MD 21702-5024

RE: John Franklin, M.D.

Dear Reviewers:

It is a pleasure to write a letter in support of the application of Dr. John Franklin for an Minority Population Focused and Collaborative Training Award. I have been acquainted with Dr. Franklin for at least 5 years, though my closer ties with him have really been established since his return to Columbia 18 months year ago. My relationship now has been both through his attending a course which I give in Cancer Epidemiology, as well as interacting with him in the design and establishment of a research program in the area of Urologic Oncology, specifically prostate cancer.

Dr. Franklin is precisely the type of individual which an award of this type should be geared to assist. He has an outstanding educational and clinical background, distinguished in anyone, but even more so for a member of a minority group. He is enthusiastic about establishing himself as an academic investigator in Urologic Oncology, and this award will provide him with the time and resources to initiate such an attempt. In particular, the area of epidemiology has lacked investigators focused on the clearcut differences between black and white men with regard to this disease, and Dr. Franklin's proposal to meld together basic, chemical, clinical, and epidemiologic science into an integrated proposal is a worthy one. Molecular epidemiology has clearly been an area of increased research interest over the past several years, and I believe that Dr. Franklin is likely to make major contributions in this area, particularly as it relates to prostate cancer.

At the present time, I serve as the Director of Cancer Prevention and Control for the Herbert Irving Comprehensive Cancer Center here at Columbia, and am also director of a T32 Training Grant overseeing 10 pre-doctoral and post-doctoral trainees along with my colleagues here. The existence of this training program in particular will give Dr. Franklin a group which with to interact. Furthermore, I have worked in the past with Dr. Ralph Buttyan, Dr. Franklin's other mentor in this proposal, and I believe the idea of having a mentor from each of the two major disciplines involved in this proposal is an outstanding one. He will have the opportunity to draw on both our expertise and to learn about collaborative research, one of the most difficult skills to

acquire.

The study of differences between whites and blacks with regards to prostate cancer with a particular focus on the separation of blacks into different national origins is superb. I know of little research, particularly on a genetic level, which has attempted to focus on this, and the opportunity to study different black populations should be a very powerful one in being able to distinguish between genetic and environmental factors. I know of no other community where such a research project can be conducted as easily or fruitfully, given the large number of immigrants from each of the populations described in the study.

Clearly, it will be difficult to accomplish a full study of these issues in the one year which this proposal would fund. However, all projects must begin at the beginning, and this award would allow Dr. Franklin to initiate the relationships and pilot projects which would ultimately lead to large scale RO1 and other types of funding. Given his background, idealism, intelligence and enthusiasm, I have little doubt that he will establish himself successfully as a major force in the area of prostate cancer research. I am looking forward with anticipation to working with him as he starts out on his academic career path.

If I can help the Committee in any other way, please feel free to contact me at (212) 305-9414 or at FAX number (212) 305-9413.

Sincerely,

Alfred I. Neugut, M.D., Ph.D. Associate Professor of Medicine

Merget, M.S., P.R.D.

and Public Health (Epidemiology)

AIN:nc

Ralph Buttyan, Ph.D. Director Molecular Urology Laboratory Columbia University College of Physicians and Surgeons Department of Urology Atchley Pavilion 11th Floor 161 Fort Washington Ave. New York, NY 10032

(212) 305-1574 (Office) (212) 305-1564 (FAX) rb46@columbia.edu (e-mail)

March 5, 1999

Dr. John Franklin
Department of Urology
Columbia University
Atchley Pavilion 11th Floor
161 Fort Washington Ave.
New York, NY 10032

Re: Your application for a Minority Population Focused Collaborative Training Award from the Department of Defense.

Dear John.

I am writing to establish my collaboration in conducting the studies outlined in your application for the Minority Population Focused Collaborative Training Award from the Department of Defense. I offer my dedicated assistance, advice and access to laboratory facilities so that these studies can be performed. I believe that based on your access to sizable and defined minority specimens for analysis will enable us to complete these studies and evaluate whether the genetic markers (CpG repeats in Androgen Receptor, Polymorphisms in Apo J, Polymorphisms in Cyp 3A4 and Polymorphisms in the Vitamin D receptor) might identify a predisposition to aggressive prostate cancer in minority populations.

Based on our review of the technical requirements for these experiments, I believe we can complete the project as you have outlined during a year. I look forward to working with you on this project and I wish you luck in obtaining funding for your straightforward project that has the potential of identifying genetic risk factors for prostate cancer in minority populations.

Regard

Ralph Buttyan, Ph.D. Associate Professor

COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS & SURGIONS HARLEM HOSPITAL GENTER

DEPAREMENT OF SURGERY

March 8, 1999

Dr. John Franklin Allen Pavilion Presbyterian Hospital 5420 Broadway New York, New York

Dear Dr. Franklin:

I have read your research proposal regarding Racial Disparity In Prostate Cancer, and I am willing to participate in your study. I can assist you by providing prostate cancer patients from Harlem Hospital Center as well as patients from my private practice at the New York Presbyterian Hospital.

Sincerely,

Gerald P. Hoke, MD MPH

Chief of Urology

GPH/bd

The Presbyterian Hospital in the City of New York Columbia-Presbyterian Medical Center, New York, NY 10032-3784

March 5, 1999

John R. Franklin, M.D. Department of Urology

Dear John:

I am excited to hear about your proposed project studying the genetic basis of the disparity of prostate cancer risk and mortality between different racial populations. I have reviewed you proposal and think that this is an excellent project. I would be enthusiastic about enrolling patients in this study. I look forward to helping you with this project. If you have any further questions, please do not hesitate to contact me at any time.

Sincerely,

Ronald D. Ennis, M.D.

RDE:jc

From: Dr Danso <danserv@harare.iafrica.com>

To: Cathy Franklin <jcfranklin@worldnet.att.net>

Date: Saturday, November 28, 1998 3:53 AM

Subject: Re: Prostate cancer research

My dear John,

I am sorry I have not been able to write earlier but believe you me , I have been thinking of you all every minute of the day . I am so happy that Asantewa is growing and becoming a big girl . I shall be able to collaborate on the research programme that you have started . Just let me know so that we can give you our input .

For the past three years as you know I have not been doing too much of the urological conferences . i had to see the boys through college and this is a whopping 60thousand dollar bill a year. Living and working in Africa it gives you no further room economically to manoevre . But Thank God , Kwabena is finishing next year . Oh how time flies !!.

The news I have for you is that I have been involved in a group which is getting an international hospital built in Accra!. The private placement document for that project has just been brought out . you cannot imagine how hectic this has been and infact I have been going to Ghana every four weeks. We acquired a 20acre piece of land in Accra and got some architects to do the drawings . The feasibility study was finished a year ago and I have been running all over the show with it . The investors have started putting in money and the construction is starting in 8weeks time . We have sunk a lot of effort and resources into this and now it is taken off . The flotation of the shares has just started so if you want to invest in Africa , there you are . We haven't met for a very long time and I am hoping that we shall meet , next year . God willing.

Mary and I are well and extremely excited at the Accra International Hospital and the fact that it has taken off so well. There is a provision for telemedicine and I am speaking to Johns Hopkins and UCIA for help. We shall be leaving for Accra on the 23rd of December to spend the Christmas at home and this year we shall be spending it as a full family because the boys are meeting us in Ghana.

Cathy, Kwabena is finishing in May 1999and would be majoring in Math and economics, please give him some guidance because he would like to go to business school, my thinking was for him to come to Africa for a few years before going to do the MBA but he is not keen in returning to Africa and yet remaining in the US and doing a good job is most difficult. Please do guide us all now and then when you have the time. We are all dying to see you and especially Asantewa, my love to all of you

Best of wishes . Love Danso .

From: Cathy Franklin <<u>jcfranklin@worldnet.att.net</u>>
To: Alex Danso <<u>danserv@harare.iafrica.com</u>>

Subject: Prostate cancer research

Date: Monday, October 19, 1998 5:16 PM

Hi Alex,

How are you and Mary? It was real nice hearing from you both. Cathy, Asantewa, and I are going through all the growing pains of a working family with a young child. My experience at Columbia University is beginning to take some shape. As you know it does take time to build a practice. I have been awarded a Department of Defense Grant to do a pilot project. I propose to evaluate the genetic basis of the racial/ethnic differences of prostate cancer. I am looking at the CAG gene, the Vit D gene, and the APO J/Clusterin gene among others. I have propose not only to look at differences between whites and blacks, but also to look at differences between black Americans and blacks from the Caribbean and Africa. I have listed you as one of my contact persons in Africa for collaboration and for potential samples. I am now in the process of writing my IRB proposal so that I can get started.

This is an ambitious project. I have secured to support of Dr. Olsson as well as the director of the urology research lab (Dr. Ralph Buttyan) and an established cancer epidemiologist (Dr. Alfred Neugut). Dr. Neugut is an Associate Professor with the Columbia University School of Public Health. I look forward to discussing this project with you some. As you can see, Alex and Mary, our lives have gotten real busy/crazy. In addition to getting the research of the ground I am doing my MPH in epidemiology. But then again Alex, you are planning or have begun to pursue a MBA Ha! Ha! I think that if we continue to apply ourselves to the cause we will get somewhere.

Love always

John and Family.

Asantewa had a wonderful time for her birthday. She cried when we sang the Happy Birthday song.

Appendix E

Detailed Cost Estimate Forms

Principal Investigator (last, first, middle)

DETAILED BUDGET FOR I			b D		1	FROM	THROUGH
Personnel				%	DOLLAR AMOUNT REQUESTED (OMIT		(OMIT CENTS)
Name	ROLE ON PROJECT	APPT. (MONTHS)			SALARY REQUESTED	FRINGE BENEFITS	TOTALS
John Franklin	Principal Investigator	12	46,350	25%	11,588	3,024	14,612
Ralph Buttyan	Collab- erator	12	867100	5%	4,305	1,124	5429
Alfred Neugut	W	12	125,900) 5%	6,295	1,642	7,937
Yi-Chen Cao	Senior Technici	an 12	35,598	3 5	3,559	929	4,488
						V-1,	
SUBTOTALS	5		<u>'</u>				\$ 32,466
CONSULTANT COSTS							
MAJOR EQUIPMENT (ITEMIZE)							·
MATERIALS, SUPPLIES, AND CON	SUMABLES (ITI	EMIZE BY CA	TEGORY)				0.200
TRAVEL COSTS							9,290
RESEARCH-RELATED PATIENT CO	OSTS	•					
OTHER EXPENSES (ITEMIZE BY C	ATEGORY)						2,232
SUBTOTAL OTHER DIRECT COS	TS FOR INITIAL	L BUDGET PI	ERIOD → → -	+++	·	→	\$11,522
DIRECT COST					11/300		
CONSORTIUM COSTS INDIRECT COST							
TOTAL PERSONNEL & OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD					\$43,988		
TOTAL INDIRECT COSTS FOR INITIAL BUDGET PERIOD					\$31,011		
TOTAL COSTS FOR INITIAL BUDGET PERIOD					^{\$} 74,999		

Salary support: Salary support is requested for the principal investigator of this project, Dr. John Franklin, Assistant Professor of Urology at Columbia University. Following his residency at Columbia University, Dr. Franklin completed a 2 years Urologic Oncology Fellowship at UCLA School of Medicine. He is also nearing completion of a MPH degree in epidemiology at Columbia University. Dr. Franklin is requesting 25% support. Dr. Franklin will combine his clinical, basic research, and epidemiologic experiences to design and execution of the project. He will establish subject eligibility, ascertain the relevant demographic data. He will be responsible for the collection of bloods as well as its delivery to the laboratory for processing. Dr. Franklin will prepare the blood samples and perform PCR analyses on the DNA products. He will be responsible for data management and analysis, and the preparation of manuscripts for publication describing the work accomplished. We are requesting 5% support for Dr. Ralph E. Buttyan, Associate Professor of Pathology and Urology at Columbia University. Dr. Buttyan, as Director of the Molecular Urology Laboratory, has spent the past 12 years studying the cellular mechanisms by which androgens control prostate cancer cell growth and survival as well as applying this knowledge to the study of hormone resistant prostate cancer. It was his experimental design that led to the discovery of the T6 marker in apoptosis-resistant prostate cancer cell lines and he continues to supervise the project and design the experimentation to allow characterization of this unique gene product. As co-mentor, Dr. Buttyan will assist the applicant in organization of the research project. Dr. Buttyan will also be responsible for overseeing the design of experimentation, ensuring that the project work meets the schedule described, regularly review the data obtained in the project and participate in the preparation of manuscripts for publication describing the work accomplished. We are requesting 5% support for Dr. Alfred I. Neugut, Associate Professor of Medicine: Oncology Division, and the School of Public Health at Columbia University. Dr. Neugut has a vast experience in both clinical and epidemiologic research in breast and colon cancer. As co-mentor, Dr. Neugut will assist in the planning and design of the study. He will also be responsible for overseeing management and analysis of data, ensure that the project work meets the schedule described, and participate in the preparation of manuscripts for publication describing the work accomplished. We are also requesting 10% support for Yi-Chen Cao, Senior Technician in Dr. Buttyan's laboratory. She is experienced in PCR, and will assist Dr. Franklin run the RT-PCR project.

All personnel expect an annual 3% increase in salary beginning on July 1, 1999, except Yi-Chen Coa who will receive a 3.5% salary increase on October 1, 1999. The indicated salaries are all adjusted to reflect these salary increases.

Fringe benefits for Columbia University officers and staff are set at 26.1% based on the policy of Columbia University and through an agreement with the Office of Naval Research.

Materials, Supplies and Consumables:

We request \$4,500.00 for oligonucleotide primers synthesis cost and PCR related supplies. We request \$2,000 for films, filters, gel, and gel supports. We request \$2,000.00 for sterile plastic ware, glassware and pipettes. We also request \$790.00 for blood collection tubes, needles, and syringes, sterile gauze, and sterile alcohol swabs.

Other Expenses: We are requesting \$2,232.00 for tuition costs so that the applicant may complete his studies for a MPH in epidemiology at the Joseph L Mailman School of Public Health, Columbia University. The applicant will take a course in epidemiology.

Indirect Costs: Indirect costs for government-sponsored research on the Columbia University Health Sciences Campus are set at 70.5% on a modified direct cost basis (not including equipment costs) as agreed to with the Office of Naval Research (dated 06/04/97).

Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 5



Federation of American Societies for Experimental Biology

—— Quality Life Through Research——

Member Societies

The American Physiological Society

American Society for Biochemistry and Molecular Biology

American Society for Pharmacology and Experimental Therapeutics

American Society for Investigative Pathology

American Society for Nutritional Sciences

The American Association of Immunologists

The American Society for Cell Biology

Biophysical Society

American Association of Anatomists

The Protein Society

The American Society for Bone and Mineral Research

American Society for Clinical Investigation

The Endocrine Society

The American Society of Human Genetics

Associate Members

Society for Developmental Biology

American Peptide Society

Association of Biomolecular Resource Facilities

Society for the Study of Reproduction

Teratology Society

Sidney H. Golub, Ph.D. Executive Director and Principal Investigator

FASEB MARC Program Minority Access to Research Careers Jacquelyn Roberts Associate Program Director

9650 Rockville Pike Bethesda, Maryland 20814-3998 Telephone 301-530-7020 FAX 301-571-0699 email: marc@faseb.org July 19, 1999

Dr. John R. Franklin Columbia Presbyterian Medical Center Department of Urology 5141 Broadway New York, New York 10034

Dear Dr. Franklin:

The Federation of American Societies for Experimental Biology/MARC Program and the Grant Writers' Seminars and Workshops, LLC jointly seek applicants for an intensive educational program. This program is designed to enhance grantsmanship skills and thereby successfully compete for NIH funding. Application for this workshop is available to participants of the "Write Winning Grants" Seminars held in 1999 (also known as Phase I).

The Phase II Grant Writing Workshop will be held on <u>November 19-22</u>, 1999 in <u>Tucson</u>, <u>Arizona</u>. The program will span approximately six months and will encompass everything from idea development through construction and submission of an application for funding.

- Develop/refine ideas for applications and assist with preparation of specific aims section
- Collectively critique and refine specific aims sections, using a workshop format
- Preparation of full drafts of applications
- Review applications for grantsmanship and scientific merit prior to submission
- Submit applications and monitor subsequent funding decisions

The instructors (Drs. Stephen W. Russell & David C. Morrison), have extensive experience in teaching others how to write grant applications. Their mission is to help investigators achieve their full potential in research, by providing them with grant-writing skills that are necessary to maximize their abilities to generate novel, innovative ideas, and to communicate those ideas effectively to grant review panels.

-continued-

There will be a total of 24-30 (3 groups of 8-10) participants selected for the Phase II Grant Writing Workshop. Each group will be assigned a full day (½ day to group with the presenter/consultant and another ½ day for a one-on-one session with the consultant). The enclosed application form must be completed and mailed. Incomplete forms will be returned.

Your application must be received by this office no later that close of business day on <u>Friday, August 13, 1999</u>. Notification of the acceptance into the Phase II Grant Writing Workshop will be announced no later than August 25, 1999.

Please be advised that successful applicants to the Phase II Grant Writing Workshop will be required to contribute all or a portion of the round-trip airfare to and from the November 1999 Workshop in Tucson, Arizona. All other expenses (ground transportation to and from home-airport-hotel, Grant Writing Workshop registration fees of \$1,500.00, meals and lodging) will be funded by the FASEB/MARC Program. Hotel accommodations will be arranged by the FASEB/MARC Program office.

For additional information, contact Ms. Ana August at 301-530-7020 or aaugust@faseb.org.

Sincerely,

Ana August

FASEB/MARC PROGRAM

/aa

encl:

Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 6







Department of Urology

College of Physicians and Surgeons of Columbia University

John R. Franklin, M.D. Assistant Professor **Squier Urological Clinic**

The Presbyterian Hospital in the City of New York

Tel: (212) 932-5526 Fax: (212) 932-5466

Dear participant:

Thank you for agreeing to participate in this study. Briefly, this study will evaluate genetic risk factors for prostate cancer in black and white males. The following questionnaire addresses several items about your personal and family history. The entire survey should take no more than 20 minutes. Read the questions carefully before answering. There are many items with multiple choices. When responding to these items, select the answer that best applies to you. Where indicated, the number matching your response should be placed in the box provided.

Example: What is your marital status? (DQ12)

4

- (1) Married or living as married (with partner)
- (2) Widower
- (3) Divorced
- (4) Separated
- (5) Never married

Select and enter the number $\underline{4}$ in the box if your marital status is separated Again, thank you for participating in this study

Sincerely,

John Roland Franklin, M.D.

Study Qu	estionnaire		
Subject Co	ode Number:		_ (DQ0) [LEAVE BLANK]
Date of Su	ırvey:		
*Do Not N	Aark Above T	his Line	
·			
1. What i	s your Name?		
Last N	ame		First Name
Middle	Initial	_(DQ1)	
2. What is	s your date of	birth?	
Month	Day	Year	
(DQ2a)	(DQ2b)	(DQ2c)	
3. What is	s your place of	birth?	
City			State
Country	y		(DQ3)

4.	. Where did you receive your schooling? Select the number and place in box. (DQ4a)					
	Caribbean =1	US = 2 Latin	n America = 3	Africa = 4	Other = 5	
	[If born in the	e <u>US,</u> skip to question	#5]			
4b	. If you went to scl	hool in the Caribbean	ı, how far did yo	ou go in scho	ool?	
Inc	licate last complet	ed year of school from	n choices below:		DQ4b). Then	go to question #6
	(0) (1) (2) (3) (4) (5) (6) (7) (8) (9) (10) (11) (12) (13) (14)	Did not go to school ABC/1 st year (age 5) 2 nd year (age 6) Standard 1 (age 7) Standard 2 (age 8) Standard 3 (age 9) Standard 4 (age 10) Standard 5 (age 11) Form 1 (age 12) Form 2 (age 13) Form 3 (age 14) Form 4 (age 15) Form 5 (age 16) Lower 6 (age 17) Upper 6 (age 18)		n. [Specify	the Country: _]
Co	llege					
	(15) (16) (17) (18)	Freshman Sophomore Junior Senior				
Gr	aduate School					
	(19) (20) (21) (22) (23)	1 year post graduate 2 years post graduate 3 years post graduate 4 years post graduate More than 4 years po	e e			

, ,

(Please see list below and indicate last completed year of schooling in box) (DQ5a) (0) Did not attend school in the US. [Specify the country:	5. If you went to school in the US, how far did you go i		o school in the US, how far did you go in school?
Crade school		(Please see li	st below and indicate last completed year of schooling in box) (DQ5a)
Crade school			
(1)		(0)	Did not attend school in the US. [Specify the country:
(3) 3 rd (4) 4 th (5) 5 th (6) 6 th Junior High (7) 7 th (8) 8 th High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 3 years post graduate (20) 4 years post graduate	Gı	ade school	· · · · · ·
(3) 3 rd (4) 4 th (5) 5 th (6) 6 th Junior High (7) 7 th (8) 8 th High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 3 years post graduate (20) 4 years post graduate		(1)	1 st grade
(3) 3 rd (4) 4 th (5) 5 th (6) 6 th Junior High (7) 7 th (8) 8 th High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 3 years post graduate (20) 4 years post graduate		(2)	2^{nd}
(4) 4 th (5) 5 th (6) 6 th Junior High (7) 7 th (8) 8 th High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 3 years post graduate (20) 4 years post graduate			
(5) 5 th (6) 6 th Junior High (7) 7 th (8) 8 th High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 3 years post graduate (20) 4 years post graduate			
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(7) 7 th (8) 8 th High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate			6 th
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High School (9) 9 th (10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 4 years post graduate (20) 4 years post graduate		(7)	7 th
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(10) 10 th (11) 11 th (12) 12 th College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (19) 4 years post graduate	Hi	gh School	
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College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate			10 th
College (13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate			
(13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate			
(13) Freshman (14) Sophomore (15) Junior (16) Senior Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate	Co	llege	
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Graduate School (17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate			
(17) 1 year post graduate (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate		(16)	Senior
 (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate 	Gr	aduate Schoo	ol Communication of the Commun
 (18) 2 years post graduate (19) 3 years post graduate (20) 4 years post graduate 		(17)	1 year post graduate
(19) 3 years post graduate(20) 4 years post graduate			
(20) 4 years post graduate			
(21) More than 4 years post graduate		(21)	More than 4 years post graduate

Di	d you earn a High	School Equivalency Degree? [No = 0)	Yes = 1]	
			(DQ5b)		
						
6.	What is the high	est degree obtained?	(DQ6)			
	(1) (2) (3) (4) (5) (6) (7)	Less than High school High school Vocational or Technical school Community College or Junior Colleg Bachelor's Degree Masters Degree Doctoral Degree	ge			
7.	What is your ma	rital status? (DQ7)				
	(1) (2) (3) (4) (5)	Married or living as married (with partied) Widower Divorced Separated Never married	artner)			
8.	If you were not b	porn in the United States, how old were	e you wh	nen you i (DQ8)	mmigrated	to the <u>US</u> ?
9.	How many years	s have you lived in the <u>US</u> ? (DQ9)				

.

10. What race or ethnic group do you consider yourself a member of? (Insert the number matching					
your ethnicity from the choices below)		(DQ10)			
(1) African-American (2) Asian (3) Haitian (4) Jamaican (5) Trinidadian (6) Dominican Republic (7) Grenadian (8) Puerto Rican (9) Barbadian (10) Bahamian (11) Dominican (Dominica)	(12) Martiniquan (13) Guadalupian (14) St. Lucia (15) Russian, Jewish (16) Russian, Non-Jewish (17) Jewish, US-born (18) Polish (19) St. Vincentian (20) Irish (21) Spaniard (22) Guyanese	(22) German (23) Austrian (24) French (25) Italian (26) Portuguese (27) Panamanian (28) English (29) Greek (30) Arab (31) Israeli (32) American Indian (33) Indian Subcontinent			
11. What race or ethnic group do you belon	ng to? (DQ11)				
(1) White (2) Black American (3) Black Caribbean (4) Black continental Af (5) Non-white Hispanic (6) Non-white Hispanic (7) Non-white French Continental (8) Other (specify)	(Caribbean) (Latin American) aribbean	our athnicity below in the boyl			
12. What is the ethinolty of your father: [11	insert the number matering ye	(DQ12)			
 (1) African-American (2) Asian (3) Haitian (4) Jamaican (5) Trinidadian (6) Dominican Republic (7) Grenadian (8) Puerto Rican (9) Barbadian (10) Bahamian (11) Dominican (Dominica) 	(12) Martiniquan (13) Guadalupian (14) St. Lucia (15) Russian, Jewish (16) Russian, Non-Jewish (17) Jewish, US-born (18) Polish (19) St. Vincentian (20) Irish (21) Spaniard (22) Guyanese	(22) German (23) Austrian (24) French (25) Italian (26) Portuguese (27) Panamanian (28) English (29) Greek (30) Arab (31) Israeli (32) American Indian (33) Indian Subcontinent			
(34) Other	r (specify)				

13. In what country was your father	born? [insert the number corresponding	g to the country below]
		(DQ13)
 (3) African Coun (4) English Speal (5) Spanish Speal (6) French Speak (7) Latin American (8) Other [Specification of the county of	antry [Specify] try [Specify] king Caribbean [Specify] king Caribbean [Specify] ing Caribbean [Specify] an [Specify] y]	
14. What is the ethnicity of your mo	ther? [insert the number corresponding	(DQ14)
 (1) African-American (2) Asian (3) Haitian (4) Jamaican (5) Trinidadian (6) Dominican Republic (7) Grenadian (8) Puerto Rican (9) Barbadian (10) Bahamian (11) Dominican (Dominican) 	(12) Martiniquan (13) Guadalupian (14) St. Lucia (15) Russian, Jewish (16) Russian, Non-Jewish (17) Jewish, US-born (18) Polish (19) St. Vincentian (20) Irish (21) Spaniard (22) Guyanese	(22) German (23) Austrian (24) French (25) Italian (26) Portuguese (27) Panamanian (28) English (29) Greek (30) Arab (31) Israeli (32) American Indian (33) Indian Subcontinent
 (3) African Cour (4) English Spea (5) Spanish Spea (6) French Speak 	untry [Specify] itry [Specify] king Caribbean [Specify] king Caribbean [Specify] king Caribbean [Specify] king Caribbean [Specify]	

16. What is the ethnicity of your Grandfa	ther? [insert the number that cor	responds to the ethnicity				
below] (DQ16)						
(1) African-American (2) Asian (3) Haitian (4) Jamaican (5) Trinidadian (6) Dominican Republic (7) Grenadian (8) Puerto Rican (9) Barbadian (10) Bahamian (11) Dominican (Dominica)	 (12) Martiniquan (13) Guadalupian (14) St. Lucia (15) Russian, Jewish (16) Russian, Non-Jewish (17) Jewish, US-born (18) Polish (19) St. Vincentian (20) Irish (21) Spaniard (22) Guyanese 	(22) German (23) Austrian (24) French (25) Italian (26) Portuguese (27) Panamanian (28) English (29) Greek (30) Arab (31) Israeli (32) American Indian (33) Indian Subcontinent				
(34) Oth	er (specify)					
17. In what country was your Grandfather born? (DQ17) (1) United States (2) European Country [Specify] (3) African Country [Specify] (4) English Speaking Caribbean [Specify] (5) Spanish Speaking Caribbean [Specify] (6) French Speaking Caribbean [Specify] (7) Latin American [Specify] (8) Other [Specify] 18. What is the ethnicity of your Grandmother? [insert the number that corresponds to the ethnicity						
below] (DQ18)						
(1) African-American (2) Asian (3) Haitian (4) Jamaican (5) Trinidadian (6) Dominican Republic (7) Grenadian (8) Puerto Rican (9) Barbadian (10) Bahamian (11) Dominican (Dominica)	 (12) Martiniquan (13) Guadalupian (14) St. Lucia (15) Russian, Jewish (16) Russian, Non-Jewish (17) Jewish, US-born (18) Polish (19) St. Vincentian (20) Irish (21) Spaniard (22) Guyanese 	 (22) German (23) Austrian (24) French (25) Italian (26) Portuguese (27) Panamanian (28) English (29) Greek (30) Arab (31) Israeli (32) American Indian (33) Indian Subcontinent 				
(34) Other	(specify)					

19. In what country was your Grandmother born? (DQ19)
(1) United States (2) European Country [Specify]
20. How tall are you now?Feet,Inches (DQ20)
21. What is your current weight? Pounds (DQ21)
22. Have you ever had a diagnosis of prostate cancer? [NO = 0, YES = 1] (DQ22) [If you answer is No to question #22, please skip to question #31]
23. How old were you when you were first diagnosed with prostate cancer? (DQ23)years
24. What was your weight when you were first diagnosed with prostate cancer?
(DQ24)Pounds 25. Did you have treatment for your prostate cancer? [NO = 0, YES = 1] (DQ25)
26. How old were you when you first received treatment for prostate cancer? (DQ26) years

,

27. What was the firs	t type of treatment you received for prostate cancer? (DQ27)
(1)	Radical Prostatectomy (Surgical removal of Prostate)
(2)	Radiation Therapy
(3)	Radioactive Seed Implantation
(4)	No Treatment/Observation
(5)	Hormonal Therapy
(6)	Removal of Testicles
(7)	Cryosurgery
(8)	Chemotherapy
(9)	Other
28. Did you receive a	second treatment for your prostate cancer? [No = 0, Yes = 1]
	(DQ28)
	question # 28, skip to question #31]
29. What was your ag	ge when you received a second type of treatment for prostate cancer?
	(DQ29)years
30. What was the sec	ond type of treatment you received for prostate cancer? (DQ30)
(1)	Radical Prostatectomy (Surgical removal of prostate)
(2)	Radiation Therapy
(3)	Radioactive Seed Implantation
(4)	No Treatment/Observation
(5)	Hormonal Therapy
(6)	Removal of Testicles
(7)	Cryosurgery
(8)	Chemotherapy
(9)	Other

. . .

31. Did anyone in	your family have prostate cancer? $[No = 0,$	Yes=1,	Do Not Know $= 2$]
		(DQ	(31)
[If you answer No	or Do Not Know to question #31, skip to ques	stion #35]	
32. Did your fathe	or have prostate cancer? [No = 0, Yes = 1, I	Oo Not Know	= 2]
		(DQ	(32)
33. How old was y	your father when he was first diagnosed with pr	ostate cancer?	,
		(DQ	(33)years
34. How many of	your brothers had or have a diagnosis of prosta	te cancer?	(DQ34)
35. How many bro	others do you have?		(DQ35)
36. Do you have a	family history of other cancers? $[No = 0]$	Yes = 1]	(DQ36)
37. What other can	ncer(s) has occurred in your family?		(DQ37)
(Circle all that	apply or put all the #'s that apply in the box)		
(1)	Breast		
(2) (3)	Lung Colon		
(4)	Bladder		
(5)	Ovarian		
(6)	Other [Specify]		
			
38. Were you adop	pted? $[No = 0 Yes = 1]$		(DQ38)

39. Informati	on on your children				
How ma	ny children do you have?	Males	Females		
		(DQ39a)		(DQ39b)	
			Total num	ber of children	n:
					(DQ39c)
40. Please inc	dicate which number repre	sents your househo	ld's total in	come before ta	ixes for the past
year, incl	uding salaries, wages, Soc	ial Security, welfar	e, and any o	ther income.	
				(DQ40)	
(1) (2) (3) (4) (5)	Less than \$9,999 Between \$10,000 and Between \$20,000 and Between \$30,000 and \$ Between \$50,000 and \$	\$29,999 49,999			
(6)	Between \$75,000 and \$	99,999			
(7) (8)	Between \$100,000 and Above \$150,000	\$149,999			
41. About ho	w much of this total house [Please indicate the numb			г	personally?
	[. 10450	or mucoming and me		50.1, (2 4 12)	
(1) (2) (3) (4) (5) (6) (7) (8)	Less than \$9,999 Between \$10,000 and Between \$20,000 and Between \$30,000 and \$ Between \$50,000 and \$ Between \$75,000 and \$ Between \$100,000 and Above \$150,000	\$29,999 49,999 74,999 99,999			•

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Smoking history

42. Have you ever been a smoker?	$[N_0 = 0]$	Yes = 1]	(DQ42a)	
		If yes: Number	L er of years	
			(DQ42)	b)
Number of pack/day	Number	r of cigarettes/day _		
(DQ4	2c)	((DQ42d)	
Do you currently smoke?	[No = 0]	Yes = 1]		
(DQ4	2e)			
Number of pack/day	_ Numbe	r of cigarettes/day _		
(DQ42	2f)		(DQ42g)	
Alcohol history 43. Do you drink Alcohol? [No = 0 Yes = 1] If no, proceed to question #48. If yes, proceed to question #44.	•	(DQ43)		
(0) Never drink beer (1) Less than once a year (2) Less than once a month (3) About one a month (4) Two or three times a mo (5) Once or twice a week (6) Three or four times a w (7) Nearly every day (8) Once a day (9) Two times a day (10) Three or more times a contraction.	onth	(DQ4)	44)	

45. How often do you drink wine?	(DQ45)	
 (0) Never drink wine (1) Less than once a Year (2) Less than once a month but at least once a year (3) About once a month (4) Two or three times a month (5) Once or twice a week (6) Three or four times a week (7) Nearly every day (8) Once a day (9) Two times a day (10) Three or more times a day 		
46. How often do you drink liquor?	(DQ46)	
 (0) Never drink liquor (1) Less than once a year (2) Less than once a month but at least once a year (3) About once a month (4) Two or three times a month (5) Once or twice a week (6) Three or four times a week (7) Nearly every day (8) Once a day (9) Two times a day (10) Three or more times a day 		
47. How many years have you been a drinker?	(DQ47)	years
48. If you do not currently drink, did you drink in the past? [No = 0	Yes = 1] (DQ48)	
49. How many years were you a drinker?	(DQ49)	years

••

50. Have you experienced baldness on the top of your head? [No	$= 0 \qquad \text{Yes} = 1]$	
•	(DQ50a)	
Approximately how many years have you experienced bal	dness on the top of your h	ead
	(DQ50b) Ye	ears
51. Do you have a history of baldness in your family? [No = 0	Yes = 1]	
	(DQ51)	

THE END

We appreciate the time and commitment that you have made to contribute to this study. For this, please accept our deepest thanks.

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Project: Race/Ethnic Based Genetic Variations in Human Genes: Defining the Genetic Evidence for Disparity of Prostate Cancer Risk and Mortality Between Different Populations.

Investigator: John Roland Franklin, M.D., Columbia University, New York, NY

APPENDIX 7

BEST AVAILBLE COPY

Diet Questionnaire

Developed by: Epidemiology Program Cancer Research Center of Hawai'i University of Hawai'i

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MARKING INSTRUCTIONS

- Use No. 2 pencil only.

 One is provided for your use.
- Do NOT use ink or ballpoint pens.
- Erase cleanly any answer you wish to change.
- Do NOT make any stray marks in this booklet.

These questions are about your usual eating habits DURING THE LAST YEAR. For each food group, please fill in the circle that best describes HOW OFTEN you ate those items and then fill in the circle that best describes your USUAL SERVING SIZE.

Most categories include examples. They are only suggestions, and you may not eat all of the listed items. Some ethnic foods are also listed. If you don't recognize the name, you probably don't eat that item.

For each item, please include any fresh, frozen, canned, and packaged foods you ate, such as TV dinners, frozen entrees, vegetables, or side dishes.

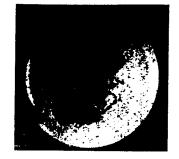
If you did not eat an item, or if you ate an item less than once a month, fill in the circle in the first column. DO NOT LEAVE BLANK. It is not necessary to choose a serving size for these items.

For some categories, pictures of food on a dinner plate are included to help you estimate your usual serving size. Please note that "1 cup" refers to an 8-ounce (240 ml.) measuring cup.

For EACH FOOD GROUP, fill in the circle O that best describes HOW OFTEN you ate those items during	ng the
last year. Then fill in the circle O that best describes your USUAL SERVING SIZE.	.:

		AV	ERAGE	USE DI	JRING L	AST YE	AR		
SOUPS, RAMEN, AND JOOK	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>	YOUR USUAL SERVING SIZE
Cream Soup or Chowder	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR Small bowl (about 1 cup) O Large bowl (2 cups or more
Dried Bean or Pea (Legume) Soup (such as Portuguese bean, split pea)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR Small bowl (about 1 cup) Ol Large bowl (2 cups or more
Tomato or Vegetable Soup (may include meat, poultry, or fish)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR Small bowl (about 1 cup) Ol Large bowl (2 cups or more
Miso Soup	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR Small bowl (about 1 cup) Ol Large bowl (2 cups or more
Broth with Noodles or Rice (such as beef noodle, chicken rice, won tun mein)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ 1/2 cup or less OR ○ Small bowl (about 1 cup) Ol ○ Large bowl (2 cups or more
Mexican Meat Soup or Stew (such as menudo, albondigas, cocido, pozole)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ 1/2 cup or less OR , ○ Small bowl (about 1 cup) OI ○ Large bowl (2 cups or more)
Ramen or Saimin (Oriental noodles with broth)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ 1/2 cup or less OR ○ Small bowl (about 1 cup) OI ○ Large bowl (2 cups or more)
Jook (rice gruel - may include meat, poultry, fish, or	0	0	0	0	86	0	0	0	CHOOSE ONE 1/2 cup or less OR Small bowl (about 1 cup) Of

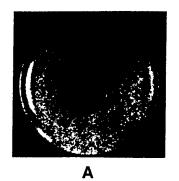


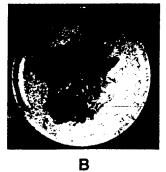




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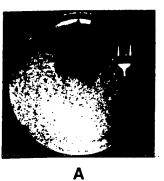
		AV	AST YE	AR					
NOODLES, SPAGHETTI, AND MIXED DISHES	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE
Chow Mein, Chow Fun, or Yakisoba (Oriental fried noodles)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) OR Photo B (about 1 cup) OR Photo C (2 cups or more)
Spaghetti, Ravioli, Lasagna, or Other Pasta with Tomato Sauce	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) OR Photo B (about 1 cup) OR Photo C (2 cups or more)
Macaroni and Cheese or Other Pasta and Cheese Casseroles	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) OR Photo B (about 1 cup) OR Photo C (2 cups or more)
Macaroni or Potato Salad (with mayonnaise)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/2 cup or less) OR ○ Photo B (about 1 cup) OR ○ Photo C (2 cups or more)
Pasta or Somen Salad	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/2 cup or less) OR ○ Photo B (about 1 cup) OR ○ Photo C (2 cups or more)
Noodle Casseroles (with tuna, chicken or turkey)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) OR Photo B (about 1 cup) OR Photo C (2 cups or more)
Pasta with Cream Sauce (such as linguine with clam sauce, beef stroganoff)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) OR Photo B (about 1 cup) OR Photo C (2 cups or more)
Arroz Con Pollo (rice with chicken)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) OR Photo B (about 1 cup) OR Photo C (2 cups or more)
Stew, Curry, Pot Pie or Empanada (with beef or lamb)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or 1 Empanada) OR Photo B (about 1 cup or 1 pie) OR Photo C (2 cups or more)
Stew, Curry, Pot Pie or Empanada (with chicken or turkey)	0	0	0		0	0	0	0	CHOOSE ONE Photo A (1/2 cup or 1 Empanada) OR Photo B (about 1 cup or 1 pie) OR Photo C (2 cups or more)

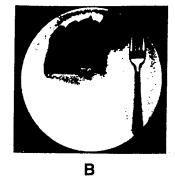


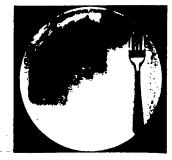




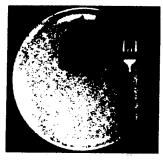
		AV	ERAGE	USE DI	JRING L	AST YE	AR		
MIXED DISHES	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE
Stir-Fried Beef or Pork and Vegetables, or Fajitas (such as beef broccoli, pork tofu, chop suey, sukiyaki)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) Photo B (about 1 cup) O Photo C (2 cups or more
Stir-Fried Chicken and Vegetables, or Fajitas (such as sukiyaki, nishime, chicken long rice)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/2 cup or less) Photo B (about 1 cup) O Photo C (2 cups or more
Stir-Fried Shrimp or Fish and Vegetables	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/2 cup or less) ○ Photo B (about 1 cup) O ○ Photo C (2 cups or more
Stir-Fried Vegetables (no meat)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/2 cup or less) ○ Photo B (about 1 cup) O ○ Photo C (2 cups or more)
Pork and Greens or Laulaus	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/2 cup or less) ○ Photo B or 1 laulau OR ○ Photo C or 2 laulaus or r
Chili	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR Small bowl (1 cup) OR Large bowl (2 cups or mc
Hamburgers (on a bun)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 regular size burger OR 1 quarter-pound burger C 1 large double burger
Cheeseburgers (on a bun)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ 1 regular size burger OR ○ 1 quarter-pound burger C ○ 1 large double burger
Meat Loaf, Meatballs, or Patties (not fast-food hamburgers)	0	0	, 0	0	0	0	0	0	CHOOSE ONE 1 to 2 meatballs OR 1 patty or slice or 3 meatballs 1 large patty or 5 meatballs
Pizza	0	0	0	0	0	0	0	0	CHOOSE ONE 1 piece or slice or less OF 2 to 3 pieces OR







		AV	ERAGE	USE DI	JRING L	AST YE	AR		
MEATS (NOT PART OF MIXED DISHES)	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE
Beef Steak or Roast, Veal or Lamb (includes beef teriyaki, chile colorado and carne asada)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B (3 oz. or 1 lamb chop) OR Photo C (5 ounces or more)
Shortribs	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B (or 2 shortribs) OR Photo C (or 3 ribs or more)
Corned Beef (fresh or canned)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B (or 1/4 12-oz. tin) OR Photo C (or 1/2 12-oz. tin or more)
Corned Beef Hash	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A or 1 patty OR Photo B or 2 patties OR Photo C or 3 patties or more
Pork Chops or Roasts, Kalua Pig, or Carnitas (includes chile verde)	O	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B (3 ounces) OR Photo C (5 ounces or more)
Ham (includes baked, fried, or sandwich)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B (3 ounces) OR Photo C (5 ounces or more)
Ham Hocks or Pig's Feet	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B (3 ounces) OR Photo C (5 ounces or more)
Spareribs	0	0	0	0	0	0	0	0	CHOOSE ONE 3 small or 1 long rib or less OR 2 to 3 long ribs (5-7 inches) OR 4 long ribs or more
Liver	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or less) OR Photo B or 3 chicken livers OR Photo C (5 ounces or more)
Chicken or Turkey Wings	0	0	0	0	0	0	0	0	CHOOSE ONE 2 chicken wings or less OR 3 chicken wings OR 1 turkey or 4 chicken wings or more







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DOM TOV AND FIGUR		AV	ERAGE	USE D	URING I	LAST YE	EAR		
POULTRY AND FISH (NOT PART OF MIXED DISHES)	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>	YOUR USUAL SERVING SIZE
Fried Chicken (includes fried chicken sandwich, nuggets)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (or 1 drumstick) Photo B (or 1 breast, 2 ti 3 wings, or 1 sandwich) Photo C (or 2 breasts or 4
Roasted, Baked, Grilled or Stewed Chicken (includes grilled chicken sandwich)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (or 1 drumstick) Photo B (or 1 breast, 2 th 3 wings, or 1 sandwich) Photo C (or 2 breasts or 4
Turkey (includes roast, ground, deli-style, or sandwich)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1 ounce or le: Photo B (3 ounces) OF Photo C (5 ounces or r
Fried Shrimp or Other Shellfish (includes tempura, fried calamari or squid)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 to 3 items OR 4 to 5 items or 1/2 cup 6 items or more
Cooked, Canned, or Raw Shellfish (such as crab, squid, shrimp)	0	0	0	0	0	0	0	0	CHOOSE ONE 5-6 shrimp or 1/4 cup 0 1 crab or 1/2 cup OR 1 lobster tail or 1 cup or
Fried Fish (includes pan-fried fish, frozen fish sticks, fried fish sandwich)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (about 1 ounce) (Photo B (3 oz. or 1 sandwi Photo C (5 ounces or more
Baked, Broiled, Boiled or Raw Fish (such as red snapper, salmon, sashimi)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (about 1 ounce) Photo B (3 ounces) OF Photo C (5 ounces or r
Canned Tunafish (plain, salad, or sandwich)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/4 cup or 1/2 sandwic 1/2 cup or 1 sandwich 1 cup or 2 sandwiches
Other Canned Fish (such as salmon, mackerel, sardines)	0	0	0	0	0	0	0	0	CHOOSE ONE 3 small sardines or 1/4 cu 1/2 cup fish OR 1 cup fish or more
Salted and Dried Fish (such as ike, cuttlefish, iriko)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 slice or strip or piece 2 slices OR 4 slices or more

		AV	ERAGE	USE DI	JRING L	AST YE	AR				
PROCESSED MEATS AND MEXICAN DISHES	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE		
Bacon (includes Canadian bacon)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 slice or strip or piece OR 2 slices OR 3 slices or more		
Regular Hot Dogs (beef or pork)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 hot dog OR 1 hot dog OR 2 hot dogs or more		
Chicken or Turkey Hot Dogs or Luncheon Meats	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 hot dog or 1 slice OR 1 hot dog or 2 slices OR 2 hot dogs or 3 slices or more		
Spam, Bologna, Salami, Pastrami or Other Luncheon Meats	0	0	,	0	0	0	0	0	CHOOSE ONE 1 slice (1 ounce or less) OR 2 slices OR 3 slices or more		
Sausage (such as pork, beef, chorizo, Polish, Vienna, Portuguese, hot links)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 piece or link OR 2-3 pieces or links or 1 patty OR 4 pieces or links or more		
Tacos, Tostadas, Sopes, or Taco Salad (with beef or pork)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 item or less OR 2 items OR 3 items or more		
Tacos, Tostadas, Sopes, or Taco Salad (with chicken)	0	0	0	0	0	C	0	0	CHOOSE ONE 1 item or less OR 2 items OR 3 items or more		
Meat Burritos (includes beef and bean and other combinations)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 fast-food burrito OR 1 medium burrito OR 1 large or 2 fast-food burritos		
Vegetable or Bean Burritos, Tacos, or Tostadas (no meat)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 item or less OR 2 items OR 3 items or more		
Enchiladas with Chicken	0	0	0	0	0	0	0	0	CHOOSE ONE 1 enchilada or less OR 2 enchiladas OR 3 enchiladas or more		
Enchiladas with Beef	0	0	0	0	0	0	0	0	CHOOSE ONE 1 enchilada or less OR 2 enchiladas OR 3 enchiladas or more		
Enchiladas with Cheese, Quesadillas, or Nachos with Cheese	0	0	0	0	0	0	0	0	CHOOSE ONE 1 enchilada or small quesadilla OR 2 enchiladas or 1 serving nachos OR 3 enchiladas		
Tamales	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 tamale or less OR 1 tamale OR 2 tamales or more		
Chili Rellenos	0	0	0	, O	0	0	0	0	CHOOSE ONE 1/2 chili relleno or less OR 1 chili relleno OR 2 chili rellenos or more		

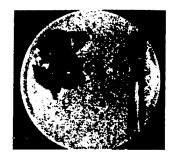
		A	VERAGI	E USE C	URING	LAST Y	EAR		
RICE, POTATOES, TARO, AND POI	Neve or hard eve	y a	times	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE
White Rice (includes musubi)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or 1 scoop or less C 1 rice bowl (1 cup) or 1 mus 2 rice bowls or 2 musubi or
Sushi or Barazushi	0	, 0	0	0	0	0	0	0	CHOOSE ONE 1-2 pieces or small cone OF 3-4 pieces or 1 large cone o cup OR 5 pieces or 1 cup or more
Brown or Wild Rice	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or 1 scoop or les 1 cup or 2 scoops OR 2 cups or more
Mexican or Spanish I	Rice	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR 1 cup OR 2 cups or more
Fried Rice	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR 1 cup OR 2 cups or more
French-Fried, Hash-Browned or oth Fried Potatoes	er O	0	0	0	0	0	0	0	CHOOSE ONE ∫ fast-food small order or 1 cup ∫ fast-food medium order OR ∫ fast-food large order or more
Mashed, Scalloped or Au Gratin Potatoes	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or 1 scoop or less 1 cup or 2 scoops OR 2 cups or more
Baked or Boiled White Potatoes	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small or 1/2 medium or less 1 medium (about 5 inches) 0 1 large potato or more
Yellow-Orange Sweet Potatoes or Yams	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small or 1/2 medium or less 1 medium (about 5 inches) Of 1 large potato or more
White or Purple Sweet Potatoes	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small or 1/2 medium or less 1 medium (about 5 inches) Of 1 large potato or more
Taro	0	0	0	0	0	0	0	0	CHOOSE ONE 1/4 taro or less OR 1/2 taro OR 1 whole taro or more
Poi	0	0	0	0	0	0	0	0	CHOOSE ONE 1/4 cup or less OR 1/2 cup OR



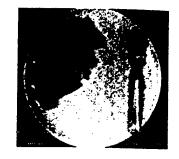




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SALAD ITEMS 500			A	VERA	IGE I	USE	DURII	VG I	AST	VEAD	<u>-</u>	-	C
SALAD ITEMS, EGO AND OTHER NON-MEAT ITEMS	ha ev	ever or rdiy ver	Oncil a month	2 t	o 3 les	Once a week	e 2 t	o 3 nes a	4 to time:	6 o	nce a lay	2 or more times	SERVING SIZE
Light Green Lettuce of Tossed Salad (such as iceberg or head lettuce)	ı)	0	C)	0		>	0		O	0	CHOOSE ONE O Photo A (1/2 cup or less) O Photo B (about 1 cup) OR
Dark Green Lettuce (such as romaine, red, butter, manoa, endive)	C		0	0		0	C)	0			0	CHOOSE ONE O Photo A (1/2 cup or less) O Photo B (about 1 cup) OB
Tomatoes	C	,	0	0		0	0		0	C)	0	CHOOSE ONE 2 slices or wedges or 2 cherry tomatoes or less OR 4 slices or 1/2 medium tomato O
Colesiaw	0		0	0		0	0		0	0		0	O 1 medium tomato or more CHOOSE ONE O 1/4 cup or less OR O 1/2 cup OR
Regular Salad Dressings or Mayonnaise Added to Salads	0		0	0		o	0	1	0	0		0	O 1 cup or more CHOOSE ONE O 2 teaspoons or less OR O 1 Tablespoon OR
Low-Calorie or Diet Dressings Added to Salads	0			0			0))	0		0	○ 2 Tablespoons or more CHOOSE ONE ○ 2 teaspoons or less OR ○ 1 Tablespoon OR
ggs, Cooked or Raw includes egg salad)	0			0	С)	0			0	())	○ 2 Tablespoons or more CHOOSE ONE ○ 1/2 egg OR ○ 1 egg or 1 sandwich OR
gg Substitute	0	С)	0	0		0	С)	0			O 2 eggs or more CHOOSE ONE ○ 2 Tablespoons OR ○ 1/4 cup (= 1 egg) OR
ofu oybean curd)	0	0		0	0		0	0		0	C	'	○ 1/2 cup (= 2 eggs) or more CHOOSE ONE ○ 2 cubes or 1/4 cup OR ○ 1/4 block or 1/2 cup OR ○ 1/2 block or more
getarian Meat Loaf, eatballs or Patties	0	0		0	0		0	0		0	С		CHOOSE ONE 1 to 2 meatballs OR 1 patty or slice or 3 meatballs OR 1 large patty. 5 meatballs or more







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RAW OR COOKED		AV	ERAGE	USE DI	JRING L	AST YE	AR			
VEGETABLES (NOT IN SOUPS OR MIXED DISHES)	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE	
Broccoli (raw or cooked)	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/4 cup or less) (Photo B (about 1/2 cup) O Photo C (1 cup or more)	
Cabbage (such as head, Chinese or Napa cabbage, Brussels sprouts)	.0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/4 cup or less) C Photo B (about 1/2 cup) O Photo C (1 cup or more)	
Dark Leafy Greens (such as spinach, collard, mustard or turnip greens, bok choy, watercress, chard)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/4 cup or less) C ○ Photo B (about 1/2 cup) O ○ Photo C (1 cup or more)	
Green Beans or Peas	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/4 cup or less) C ○ Photo B (about 1/2 cup) O ○ Photo C (1 cup or more)	
Other Green Vegetables (such as zucchini, celery, asparagus, green pepper, okra)	0	0	0	0	O	0	0	0	CHOOSE ONE ○ Photo A (1/4 cup or less) C ○ Photo B (about 1/2 cup) OI ○ Photo C (1 cup or more)	
Cauliflower	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/4 cup or less) O ○ Photo B (about 1/2 cup) O' ○ Photo C (1 cup or more)	
Carrots (raw or cooked)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (or 4-5 sticks or less) (○ Photo B (1/2 cup or 1 med.) O. ○ Photo C (1 cup or more)	
Corn (fresh, frozen, or canned)	0	0	0	0	0	0	0	0	CHOOSE ONE ○ Photo A (1/4 cup or less) OF ○ Photo B (1/2 cup or 1 cob) C ○ Photo C (1 cup or more)	
Pumpkin or Yellow- Orange Winter Squash	0	0	0	0	0	0	0	0	CHOOSE ONE O Photo A (1/4 cup or less) O Photo B (about 1/2 cup) Of Photo C (1 cup or more)	
Other Vegetables (such as white or summer squash, beets, eggplant)	0	0	Ó	0	0	0	0	0	CHOOSE ONE O Photo A (1/4 cup or less) O Photo B (about 1/2 cup) OF Photo C (1 cup or more)	

		AV	ERAGE	USE DU	JRING L	AST YE	AR		
DRIED BEANS (NOT IN SOUPS OR MIXED DISHES)	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>	YOUR USUAL SERVING SIZE
Refried Beans (not in burritos or tostadas)	0	0	0	0	0	0	0	0	CHOOSE ONE O Photo A (1/4 cup or less) OR Photo B (about 1/2 cup) OR Photo C (1 cup or more)
Baked Beans or Pork and Beans	0	0	0	0	0	0	0	0	CHOOSE ONE Photo A (1/4 cup or less) OR Photo B (about 1/2 cup) OR Photo C (1 cup or more)
Boiled Dried Beans or Peas (such as red, lima, pinto or soy beans, black-eyed peas, frijoles de la olla)	0	0	ó	0	0	0	0	0	CHOOSE ONE Photo A (1/4 cup or less) OR Photo B (about 1/2 cup) OR Photo C (1 cup or more)

during the

		AV	ERAGE	USE DI	JRING L	AST YE	AR		•
FRUITS AND JUICES	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE
Oranges	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 orange or 1/2 cup or less OR 1 orange or 1 cup OR 2 oranges or more
Tangerines or Mandarin Oranges	0	0	0	0	0	0	0	0	CHOOSE ONE 1 tangerine or 1/2 cup or less OR 2 tangerines or 1 cup OR 3 tangerines or more
Grapefruit or Pomelo	0	0	0	0	0	0	0	0	CHOOSE ONE 1/4 cup or less OR 1/2 grapefruit or 1/2 cup OR 1 cup or more
Papaya	0	0	0	0	0	0	0	0	CHOOSE ONE 1/4 papaya or less OR 1/2 papaya OR 1 papaya or more
Pineapple (fresh or canned)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 slice or wedge or less OR 1/2 cup or 2 slices or wedges OR 1 cup or more
Peaches (fresh, canned, or dried)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 peach or less OR 1 peach or 2 halves or 1/2 cup OR 2 peaches or 1 cup or more
Apricots (fresh, canned, or dried)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 apricot or less OR 2 apricots or 1/2 cup OR 3 apricots or more
Pears (fresh, canned, or dried)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 pear or 1/2 cup OR 1 pear or 1 cup OR 2 pears or more

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		ΔVI	ERAGE	USE DU	RING L	AST YE	AR	,	
FRUITS AND JUICES (continued)	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE
Apples and Applesauce	0	0	0		0	0	0	0	CHOOSE ONE 1/2 apple or 1/2 cup OR 1 apple or 1 cup OR 2 apples or more
Bananas	0	0	0	0	0	0	0	0	CHOOSE ONE ○ 1/2 banana OR ○ 1 banana OR ○ 2 bananas or more
Cantaloupe (in season)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/4 cantaloupe or less OR 1/2 cantaloupe OR 1 cantaloupe or more
Watermelon (in season)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 quarter slice or 1/2 cup (1 half slice or 1 cup OR 1 whole slice or more
Mangoes (in season)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup slices OR 1 medium or Pirie or 1 cup 1 large or Hayden or more
Avocados and Guacamole	0	0	0	0	0	0	0	0	CHOOSE ONE 2 slices or 2 Tablespoons (1/4 avocado or 1/4 cup OF 1/2 avocado or 1/2 cup or mo
Any Other Fruit (fresh, canned, or dried)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 cup or less OR 1 fruit or 1 cup OR 2 fruits or more
Orange or Grapefruit Juice (not orange drinks or orange soda)	0	0	0	0	0	0	0	0	CHOOSE ONE Small juice glass (1/2 cup) Large glass (8 ounces) OR 12-ounce can or more
Tomato or V-8 Juice	0	0	0	0	0	0	0	0	CHOOSE ONE Small juice glass (1/2 cup) Large glass (8 ounces) OF 12-ounce can or more
Other Fruit Juices or Fruit Drinks	0	0	0	0	0	0	0	0	CHOOSE ONE Small juice glass (1/2 cup) Large glass (8 ounces) OF 12-ounce can or more
	AVERAGE USE DURING LAST YEAR								
BREAD ITEMS	Never or hardly ever	Once	2 to 3 times	Once a week	2 to 3 times a week	T	Once a	2 or more times a day	YOUR USUAL SERVING SIZE
White Bread (includes sandwich, French, sourdough, pan dulce, Portuguese sweet bread)	+	0	,	0	0	0	0	0	CHOOSE ONE 1 slice or less OR 2 slices OR 3 slices or more
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		AVE	RAGE	USE DU	RING L	AST YE	AR		
BREAD ITEMS (continued)	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>	YOUR USUAL SERVING SIZE
Whole Wheat or Rye Bread (includes pumpernickel, whole wheat pita bread)	0	Ö	0	0	0	0	0	0	CHOOSE ONE 1 slice or less OR 2 slices OR 3 slices or more
Other Bread (such as mixed grain, oat bran, raisin bread)	0	0	0	0	0	0	0.	0	CHOOSE ONE O 1 slice or less OR O 2 slices OR O 3 slices or more CHOOSE ONE
Rolls, Buns, Biscuits, or Flour Tortillas (includes bagels, English muffins)	0	0	. 0	0	0	0	0	0	1 item or less OR 2 items or 1 bagel or English muffin OR 3 items or more
Corn Tortillas	0	0	0	0	0	0	0	0	CHOOSE ONE 1 tortilla OR 2 tortillas OR 3 tortillas or more
Corn Muffins, Cornbread, or Cornbread Stuffing	0	0	0	0	0	0	0	0	CHOOSE ONE 1 piece cornbread or 1/2 cup stuffing OR 1 muffin or 1 cup stuffing OR 2 muffins or 2 pieces cornbread or more
Bran, Blueberry or Other Muffins, Banana or Mango Bread	0	0	0	0	0	0	0	0	CHOOSE ONE 1 regular muffin or 1 slice OR 1 large muffin or 2 slices OR 3 muffins or 3 slices or more
Sweet Rolls, Croissants, Doughnuts, Danish Pastry, or Coffee Cake	0	0	0	0	0	0	0	0	CHOOSE ONE 1 item or less OR 2 items OR 3 items or more
Pancakes, Waffles, or French Toast	0	0	0	0	0	0	0	0	CHOOSE ONE 1 item or less OR 2 items OR 3 items or more
Margarine Added to Bread	0	0	0	0	0	0	0	0	CHOOSE ONE O spread thin OR spread thick
Butter Added to Bread Items	0	0	0	0	0	0	0	0	CHOOSE ONE O spread thin OR o spread thick
Peanut Butter Added to Bread Items	0	0	0	0	0	0	0	0	CHOOSE ONE O spread thin OR o spread thick
Jam or Jelly Added to Bread Items	0	0	0	0	0	0	0	0	CHOOSE ONE O spread thin OR o spread thick
Mayonnaise in Sandwiches	0	0	0	0	0	0	0	0	CHOOSE ONE O spread thin OR spread thick

AVERAGE USE DURING LAST YEAR BREAKFAST YOUR USUAL 2 to 3 2 or 4 to 6 2 to 3 Never CEREALS, MILK, Once **SERVING SIZE** Once Once more times times times or a AND CHEESE times a a hardly 8 day month week day month week week ever **CHOOSE ONE Highly Fortified Cereals** 1/2 cup or less OR (such as Product 19, Total, 1 cup or individual box OR 0 0 0 0 0 0 0 0 1-1/2 cups or more **CHOOSE ONE** 1/2 cup or less OR **Bran or High Fiber** 1 cup or individual box OR 0 0 O 0 0 0 0 0 Cereals 1-1/2 cups or more **CHOOSE ONE** 1/2 cup or less OR Other Cold Cereals 1 cup or individual box OF (such as corn flakes, 0 0 0 0 0 O Ο O Cheerios, granola) 1-1/2 cups or more **CHOOSE ONE** 1/2 cup or less OR **Cooked Cereals** (such as oatmeal, cream of 1 cup or individual packet (0 0 0 0 0 0 0 0 wheat, corn grits) 1-1/2 cups or more **CHOOSE ONE** 1/2 cup or less OR Whole Milk 1 cup or half-pint carton O (as beverage or added to 0 0 0 Ο 0 0 Ο 0 2 cups or more **CHOOSE ONE** Lowfat Milk (1% or 2%) 1/2 cup or less OR (as beverage or added to 1 cup or half-pint carton O 0 0 0 0 0 cereal - includes lactaid 0 0 Ο 2 cups or more and acidophilus milk) **CHOOSE ONE** Nonfat or Skim Milk or 1/2 cup or less OR **Buttermilk** 1 cup or half-pint carton C \circ 0 0 O 0 0 0 0 (as beverage or added to 2 cups or more cereal) **CHOOSE ONE** 1/2 cup or 4-6 oz. carton (1 cup or 8 oz. carton OR 0 0 0 0 0 0 0 0 (includes lowfat and nonfat) 2 cups or more **CHOOSE ONE** 1/2 cup or less OR Chocolate Milk, Cocoa, or 0 1 cup OR 0 0 0 0 0 0 O **Ovaltine** 2 cups or more **CHOOSE ONE** 1/2 milkshake or malt OR 1 milkshake or malt (12 oz.) 0 Milkshakes or Malts 0 0 0 0 0 0 0 2 milkshakes or malts **CHOOSE ONE** 1/4 cup or less OR **Cottage Cheese** O 1/2 cup or 1 scoop OR (includes farmer's and 0 0 O 0 O 0 0 \bigcirc ricotta cheese) O 1 cup or more CHOOSE ONE 1/2 slice OR **Lowfat Cheese** O 1 slice (1 ounce) OR (such as lowfat American, \bigcirc 0 0 0 0 0 0 0 O 2 slices (2 ounces) or mc lowfat Swiss, mozzarella) **CHOOSE ONE** O 1/2 slice or 1 Tablespoor **Other Cheese** O 1 slice (1 ounce) OR (such as American, O 0 0 0 0 0 0 0 O 2 slices (2 ounces) or mc cheddar, cream cheese)

1 16.000	AVERAGE USE DURING LAST YEAR								101101101101			
ESSERTS AND NACKS	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day	YOUR USUAL SERVING SIZE			
ce Cream	0	0	0	0	0	0	0	0	CHOOSE ONE 1 scoop (1/2 cup) or less OR 2 scoops (1 cup) or 1 bar OR 3 to 4 scoops (1 pint) or more			
ce Milk, Frozen Yogurt, or Sherbet	0	0	0	0	0	0	0	0	CHOOSE ONE 1 scoop (1/2 cup) or less OR 2 scoops (1 cup) or 1 bar OR 3 to 4 scoops (1 pint) or more			
Cookies, Brownies, or Fruit Bars	0	0	0	0	0	0	0	0	CHOOSE ONE 1 to 2 average size cookies OR 3 to 4 average or 1 extra large cookie or 1 brownie or fruit bar OR 2 large cookies or brownies or more			
Cake	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small piece or cupcake OR 1 average piece (1/12 of cake) OR 2 pieces or more			
Apple or Other Fruit Pies, Tarts, Cobblers, or Turnovers	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small piece OR 1 piece (1/8 pie) or 1 item OR 1/6 pie or more			
Pumpkin, Sweet Potato, or Carrot Pies	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small piece OR 1 average piece (1/8 pie) OR 1/6 pie or more			
Cream or Custard Pies, Eclairs, or Cream Puffs	0	0	0	0	0	0	0	0	CHOOSE ONE 1 small piece OR 1 average piece or 1 item OR 1/6 pie or more			
Puddings or Custards (includes flan)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 snack-size or 1/2 cup OR 2 snack-size or 1 cup OR 3 snack-size or 1-1/2 cups			
Chocolate Candy	0	0	0	0	0	0	0	0	CHOOSE ONE 1 to 3 pieces OR 1 regular-size bar OR 1 giant-size bar or more			
Dim Sum, such as Bao or Manapua (Chinese bun with meat and vegetables)	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 bao or less OR 1 bao OR 2 bao or more			
Other Dim Sum (such as pork hash, gau gee, fried won ton, eggroll)	0	0	0	0	0	0	0	0	CHOOSE ONE 1 to 2 pieces OR 3 to 4 pieces OR 5 pieces or more			
Crackers and Pretzels (such as soda, graham, Japanese rice crackers, wheat thins)	0	0	0	0	0	0	0	0	CHOOSE ONE 4 to 5 snack or 1 large cracker OR 6 to 10 snack or 2 large crackers Ol 3 large crackers or more			
Peanuts or Other Nuts	0	0	0	0	0	0	0	0	CHOOSE ONE 12 nuts or less OR 1/4 cup OR 1/2 cup or more			

			AV	ERAGE							
SNACKS (continued)		Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>	YOUR USUAL SERVING SIZE	
Potato, Corn, Tor Other Chips, or Chicharrones (po		0	0	0	0	0	0	0	0	CHOOSE ONE 1 snack bag or 1/2 cup OR 1-ounce bag (1 cup) OR 1/2 twin-pack or more	
Popcorn		0	0	0	0	0	0	0	0	CHOOSE ONE 1 to 3 cups or less OR 1 microwave bag OR 1 medium theater tub or more	
AVERAGE USE DURING LAST YEAR											
ALCOHOLIC AND OTHER	Never	Once	2 to 3	Once	2 to 3	4 to 6	Once	2 to 3	4 or	YOUR USUAL	

			AVERA	GE US	DURIN	IG LAST	YEAR			
ALCOHOLIC AND OTHER BEVERAGES	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 to 3 times a day	4 or more times a day	YOUR USUAL SERVING SIZE
Regular or Draft Beer	0	0	0	0	0	0	0	0	0	CHOOSE ONE 1 can or bottle or less OR 2 cans or bottles OR 3 cans or bottles OR 4 cans or bottles or more
Light Beer	0	0	0	0	0	0	0	0	0	CHOOSE ONE 1 can or bottle or less OR 2 cans or bottles OR 3 cans or bottles OR 4 cans or bottles or more
White or Pink Wine (includes champagne and sake)	0	0	0	0	0	0	0	0	0	CHOOSE ONE 1 glass or less OR 2 glasses OR 3 glasses OR 4 glasses or more
Red Wine	0	0	0	0	0	0	0	0	0	CHOOSE ONE 1 glass or less OR 2 glasses OR 3 glasses OR 4 glasses or more
Hard Liquor (such as bourbon, scotch, gin, vodka, tequila, rum, cocktails)	0	0	0	0	0	0	0	0	0	CHOOSE ONE 1 drink or less OR 2 drinks OR 3 drinks OR 4 drinks or more
Regular Sodas (such as Coca-Cola, Pepsi, 7-Up)	0	0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 can or small glass OR 1 can or large glass OR 2 cans or glasses OR 3 cans or glasses or more
Diet Sodas (such as Diet Coke, Diet Pepsi, Diet 7-Up)		0	0	0	0	0	0	0	0	CHOOSE ONE 1/2 can or small glass OR 1 can or large glass OR 2 cans or glasses OR 3 cans or glasses or more

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OTHER BEVERAGES	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	s time	es	Once a day	2 to 3 times a day	4 or mor times day	e . a	USU	ALLY DD?			
Cappuccino - 1 cup or mug (includes café au lait, caffé	0	0	0	0	0	C		0	0	0		MARK AL	r honey ubstitute			
Regular Coffee - 1 cup or mug (brewed or instant)	0	0	0	0	0)	0	0	С		MARK ALL THAT APP Cream or half & half Milk Non-dairy cream Sugar or honey Sugar substitute		half		
Decaffeinated ("Decaf") Coffee - 1 cup or mug (brewed or instant)	0	0	0	0	0) (Э	0	0	C	>	MARK ALL THAT APF O Cream or half & half Milk Non-dairy cream Sugar or honey Sugar substitute		half		
Black Tea - 1 cup or glass (such as Lipton's, oolong, iced tea)	0	0	0	0	С) (O .	0	0			MARK ALL THAT APP Cream or half & half Milk Non-dairy cream Sugar or honey Sugar substitute		half n		
Green, Herbal, or Other Tea - 1 cup	0	0	0	0	C) (0	0	0							
Fortified Diet Beverages - 1 glass or can (such as Slimfast)	0	0	0	0			0	0	С							
								AVER	AGE U	SE DU	RING I	NG LAST YEAR				
HOW OFTEN DID YOU	U EAT	THE FO	LLOWIN	1G	1	Never or hardly ever	Ond a mor	ce ti	mes	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>		
Western Pickles or Re (such as dill or sweet pi						0	С		0	0	0	0	0	0		
Olives						0	C	5	0	0	0	0	0	0		
Salsa or Hot Chili Pep	pers (red	or greer	n)			0	C	5	0	0	0	0	0	0		
Garlic	· ·					0	C	5	0	0	0	0	0	0		
Onions						0	()	0	0	0	0	0	0		
Oriental Salted or Pic (such as salted cabbage		0		0	0	0	0	0	0	0						
Seaweed (fresh or drie (such as ogo limu, furik						0	(0	0	0	0	0	0	0		
Gravy on meat, potat	oes, rice)		,		0	(0	0	0	Ö	0	0	0		

	FRAGE	AGE USE DURING LAST YEAR									
HOW OFTEN DID YOU ADD THE FOLLO TO YOUR FOODS AT THE TABLE	OWING ITEMS	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a <u>day</u>		
Salt		0	0	0	0	0	0	0	0		
Shoyu (Soy Sauce) or Teriyaki Sauce		0	0	0	0	0	0	0	0		
Mustard		0	0	0	0	0	0	0	0		
Catsup	0	0	0	0	0	0	0	0			
Sour Cream		0	0	0	0	0	0	0	0		
HOW OFTEN DID YOU EAT YOUR MEA OR FISH PREPARED IN THE FOLLOWI	T, POULTRY, NG WAYS	Never or hardly ever	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day		
Charcoal-broiled		0	0	0	0	0	0	0	0		
Oven-broiled		0	0	0	0	0	0	0	0		
Fried	0	0	0	0	0	0	0	0			
Barbecued		0	0	0	0	0	0	0	0		
			AV	ERAGE	RAGE USE DURING LAST YEAR						
HOW OFTEN DID YOU EAT MEAT, CHI	CKEN, OR	Never or hardly ever	Once a month	2 to 3 times a month	Once a <u>week</u>	2 to 3 times a week	4 to 6 times a week	Once a day	2 or more times a day		
■ Vegetable Oil		0	0	0	0	0	0	0	0		
Salt Pork, Lard, or Bacon Fat		0	0	0	0	0	0	0	0		
Vegetable Shortening (such as Crisco)		0	0	0	0	0	0	0	0		
Margarine		0	0	0	0	0	0	0	0		
Butter		0	0	0	0	0	0	0	0		
Vegetable spray, water, or non-stick pan		0	0	0		0		0	0		
ANSWER THE FOLLOWING FOR 1					\A/L1	EN VOU	ATE CL	IICKEN	DID		
WHEN YOU ATE MEAT, HOW WAS IT USUALLY PREPARED? Rare Medium Well-done Don't eat meat	AS IT USUALLY PREPARED? O Rare O Medium O Well-done YOU EAT T O Most of O Some Never						ATE CHE SKIN f the time of the tim or hardly eat chicke	e ever			
WHAT KIND OF MARGARINE DID YOU USUALLY USE? (mark only one) Regular Stick OR Regular Tub OR Diet or Spread OR Don't use margarine	WHAT KIND OF USUALLY USE? Regular C Whipped Don't use Don't kno	R Soybean or corn o OR Olive oil Outter Canola oil Any other oil				USE? (r	ABLE Condition	y one)			

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CRITICAL CONTRACTOR OF THE CRITICAL CONTRACTOR O	V	TAMINS AND	MINERALS	
	OF THE FOLLOWIN	G MULTIVITAMINS	OR MULTIVITAMINS WI	TH MINERALS DURING THE S, HOW MANY YEARS HAVE
DID YOU TAKE ANY OLD LAST YEAR (at least	once a week)?	IF YES, HUM MINIT	TABLETS IF YE	S, HOW MANY YEARS HAVE TAKEN THEM?
LAST TEATT (at 1989)		DID YOU TAKE?		year or less
	ONO	○ 1 to 3 a week○ 4 to 6 a week	O 2	to 4 years
STRESS-TABS TYPE	O No O Yes	○ 1 a day	○ 5	years or more
SIKE22-IMD3 III	. 0100	O 2 a day		-
		3 or more a da1 to 3 a week	\cup 1	year or less
	○ No	0 4 to 6 a week	\bigcirc 2	to 4 years
THERAPEUTIC,	○ Yes →	○ 1 a day	→ 05	years or more
THERAGRAN TYPE		O 2 a day	av.	
		3 or more a da1 to 3 a week	\cup	year or less
	○ No	4 to 6 a week	\cup 4	to 4 years years or more
ONE-A-DAY TYPE	○ Yes →	► ○ 1 a day	→ 0;	years or more
		2 a day3 or more a d	av	
	OF THE FOLLOW	NG VITAMINS OR M	MINERALS BY ITSELF DU	JRING THE LAST YEAR (at
least once a week)?	1			4
least office a woody		S, HOW MANY ETS DID	YEARS HAVE YOU	F YES, WHAT WAS THE DOSE PER TABLET?
	YOU.	<u> </u>		5,000 I.U. (International Units) Of less
	, i	to 3 a week	O 1 year or less	○ 6,000 to 10,000 I.U.
VITAMIN A	<u> </u>	to 6 a week a day	O 2 to 4 years	O 11,000 to 24,000 I.U.
(BY ITSELF)		a day	5 years or more	O 25,000 I.U. or more Don't know
	<u> </u>	or more a day		250 mg (milligrams) or less
		to 3 a week to 6 a week	O 1 year or less	○ 300 to 500 mg. ☐
VITAMIN C		a day -		○ 600 to 4,000 mg. ○ 5,000 to 9,000 mg.
(BY ITSELF)	02	a day	5 years or more	○ 10,000 mg. or more
	\bigcirc 3	or more a day		O Don't know
	01	to 3 a week	0.4	200 I.U. (International Units) or less 250 to 800 I.U.
VITAMIN E		to 6 a week	○ 1 year or less○ 2 to 4 years	○ 825 to 1,200 l.U.
(BY ITSELF)		a day	○ 5 years or more	○ 1,250 I.U. or more
	03	or more a day		O Don't know
	_	to 3 a week	O 1 year or less	O 6,000 mcg (micrograms) or less
BETA-CAROTENE	O 1.00	I to 6 a week I a day	O 2 to 4 years	○ 7,000 to 15,000 mcg.
(BY ITSELF)		2 a day	O 5 years or more	O 16,000 mcg. or more O Don't know
	0;	3 or more a day		○ 250 mg (milligrams) or less
	O No O	1 to 3 a week 4 to 6 a week	○ 1 year or less	
CALCIUM		1 a day →	O 2 to 4 years	○ 625 to 1,000 mg.○ 1,250 mg. or more
(BY ITSELF)	0	2 a day	○ 5 years or more	O Don't know
	$\frac{0}{0}$	3 or more a day 1 to 3 a week		○ 75 mcg. (micrograms) or less
	O No O	4 to 6 a week	O 1 year or less	○ 100 to 150 mcg.○ 200 to 225 mcg.
SELENIUM (BY ITSELF)	○ Yes → ○	1 a day	2 to 4 years5 years or more	○ 250 mcg. or more
(DITIOLLI)	00	2 a day 3 or more a day	O o your or mere	O Don't know
	0	1 to 3 a week	O 4	○ 50 mg. (milligrams) or less ○ 51 to 150 mg.
IRON	<u> </u>	4 to 6 a week	1 year or less2 to 4 years	→ ○ 151 mg. or more
(BY ITSELF)	<u> </u>	1 a day 2 a day	○ 5 years or more	O Don't know
, , , , , , , , , , , , , , , , , , ,	0	3 or more a day	-	